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OCULAR MANIFESTATIONS OF ALLERGY

J. WARRICK THOMAS, M.D., F.A.C.A.
Richmond, Virginia

SINCE the consideration of allergy as an etiologic factor in certain ocular conditions, much has been contributed to our knowledge of their management. For a long time it has been a well established fact that the eye plays a definite rôle as a shock tissue in allergy. The eye has frequently been demonstrated as a test site in such examples as: before the administration of an antiserum for scarlet fever and other infectious diseases, and as a means of testing by conjunctival tests with pollen extracts in determining individual pollen sensitivities. Over the past decade much has been written on the subject of ocular allergy. One appreciates the emphasis and wisdom of a consideration of certain ocular conditions from the point of view of allergy, especially those which do not respond to vigorous treatment by non-allergic methods. Lewis Bachman[1] has summarized significant research in this field in his discussion of the clinical manifestations of allergy in ophthalmology in "The 1941 Year Book of the Ear, Eye, Nose and Throat," and more recently Fine and Sweeney[4] have given a rather comprehensive consideration with special reference to allergic iritis. Bowen,[2] and Thomas[8,9] have considered allergic conjunctivitis as well as other ocular manifestations of allergy.

The author was privileged to be associated with Albert D. Ruedemann over a period of some five to six years and had the opportunity to observe and study unusual ocular manifestations of allergy as well as the more common types.

HISTORY

The importance of a careful history must be emphasized in the handling of these patients as this is one of the most important steps in arriving

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at an accurate diagnosis and determining the best therapeutic approach.

In the consideration of ocular manifestations of allergy, questions are directed according to the area of the eye that is involved.

AREAS OF ALLERGIC INVOLVEMENT

One must consider the anatomical structures of the eye in order that he may appreciate the areas of allergic involvement in which reactions are manifested. These can be listed as follows:

1. External eye
2. Conjunctiva
   (a) Marginal
   (b) Palpebral
   (c) Bulbar and ocular
   (d) Corneal and ocular
   (e) Corneal
3. Iris
4. Lens
5. Vitreous body
6. Retina
7. Orbit

In this discussion, we will consider the types of allergic involvement according to the anatomical areas in which they appear.

1. *External eye*

(a) *Dermatitis of the eye.*—This may be subdivided into two distinct types: (1) contact dermatitis and (2) atopic dermatitis. Both of these are primarily an involvement of the lid, although the conjunctiva as well as the cornea may be affected. One of the most frequently encountered allergic conditions of the eye is contact dermatitis which by thickening of the lids produces a fibrosis and makes the patient extremely uncomfortable, although no serious ocular defects usually develop.

Atopic dermatitis is not infrequently associated with a marked congestion of the conjunctiva and episodes of congestion accompany flare-ups where the atopic dermatitis is exacerbated. A further clinical evidence of contact dermatitis is a dry, scaly skin with or without a low grade edema and erythema which produces this definite thickening of the upper and lower eyelids which may be present over an extended period of time. At times there may be a fissuring or a tendency to weeping, particularly in the early forms. One may notice in the acute forms a definite vesiculation associated with symptoms of photophobia, ocular conjunctival congestion and rather marked lacrimation.

In contact dermatitis one must exclude etiologic agents such as cosmetics, face soaps, rouge, lipsticks, hair shampoo, toilet articles, hair preparations, skin creams, nail polish, rubber eyelash curlers, dusting powder, cleansing cream or an associated low grade eczema elsewhere. One must bring out the history of lacrimation, associated symptoms of photophobia, exclude tobacco in all forms, shaving lotions, shaving creams, sensitivity to feather pillows, woolen blankets, local medication to the

eyelids, as well as exposure to chemical and other types of fumes. Almost any substance may produce a dermatitis.

A careful investigation may reveal the cause of the local irritation and the removal of the etiologic agent is the best method of treatment. The edema of the eyelids is not uncommon in allergic patients, and usually is evident in the morning. In most instances, the edema is due to face creams left on the face overnight, or to a sensitivity to feather pillows or woolen blankets, and with the use of cold compresses and the elimination of the suspected allergen, these patients are offered considerable relief.

(b) *Blepharitis marginalis,* as the name implies, is an inflammation of the glands at the margin of the lid. This involvement may be further subdivided into two groups: (1) The *sicca,* which is a dry type with silvery scales, is seen not only in atopic and contact dermatitis but also in seborrheic dermatitis, frequently with steady invasion of staphylococcus albus. (2) The *ulcerosa,* which is ulcerated, is frequently encountered in patients who have food allergies as well as inhalant allergies. The local treatment to the lids is valueless unless the cause of the dermatitis, whether it be contact, atopic or seborrheic in type, is controlled with the subsequent disappearance of symptoms. The local treatment of this type of dermatitis consists of the removal of the seborrheic scales, the application of bland ointments such as 3 per cent ammoniated mercury, and cold compresses for the itching and burning. For the low grade conjunctivitis, a solution of zinc sulphate, gr ¼ to the ounce, with a dram of adrenalin, may be used. In the marginalis ulcerosa type an acute meibomianitis is not uncommon. In the ulcerosa type of blepharitis, in addition to a staphylococcic infection, there may be secondary invaders accompanied by an alteration of the glandular secretion from an allergic reaction which is also true of the gland of Zeiss and Moll. One certainly has to consider a bacterial sensitivity which is ever present in the conjunctival secretion in varying amounts and toxicity. The use of such antibiotics as ophthalmic Aureomycin Ointment and other similar types are worthy of consideration.

(c) *Chalazion* is a small acute cyst which develops in the lid and which may or may not rupture through the natural opening upon the lid margin. When it ruptures through the gland canal, it usually disappears although a permanent small, hard, granular nodule may form and require incision and curettage subsequently.

(d) *Hordeoli, or styes,* are infections of the glands of Zeiss and Moll and are usually one of two types: (1) Those which come rapidly to a head containing a small central mass of usually green pus and a core, and which disappear after the infection is over and (2) those that are more chronic, develop slowly, are painful and contain mucopurulent sebaceous material and may persist over a period of several days. The second type is believed to be a manifestation of allergy plus a secondary infection and these have a tendency to recur, sometimes frequently. These may be caused

by food sensitivity, although it is not infrequently associated with sensitivity to inhalants as well as pollen.

2. *Conjunctiva*

(a) *Conjunctivitis* is the most frequent manifestation of ocular allergy, presenting symptoms of lacrimation, photophobia and a tendency toward blepharospasm. Many of these patients describe the sensation of having sand in their eyes. Fine, grit-like granules, which occasionally swell and have a predilection for the under surface of the outer and inner thirds of the upper lid, are frequently observed. They may be chronic and of increased severity, and follicles may appear. In the acute attacks of allergic conjunctivitis such as observed after brief exposure to an allergen, one might note flare-ups in periods of a few hours to a few days. Such a reaction is not uncommon in persons who are using a different brand of cosmetics for the first time, or who have had a slight irritation of the eye from some local medication.

In allergic conjunctivitis the tissues react to usually innocuous stimuli with an abnormal response which may be a part of a general anaphylactic process. They may also exhibit a marked local sensitization upon immediate contact with an allergen. In the more severe forms there may be a sudden, extreme vascular dilatation accompanied by a bloody exudated type of inflammation. This may be controlled or the inflammation may resolve following the removal of the irritant, but is followed in chronic cases by a cellular infiltration and finally new connective tissue formation. The presence of eosinophiles is an indication of allergic conjunctivitis, although many times smears may be made in which eosinophiles are not demonstrated; therefore, it is necessary to make repeated smears as frequently one might observe showers of eosinophiles during an acute exacerbation.

In chronic conjunctivitis the conjunctival sac is usually sterile and this type may be associated with a foci infection elsewhere in the body. The onset is usually gradual and the mucosa becomes quite red and boggy with a little watery secretion, and constant irritation and itching may be accompanied by an infection in the nose and nasal pharynx and tonsils. Treatment is usually palliative and local. One finds astringents such as epinephrine, ephedrine and cocaine, as well as ophthalmic analgesic ointments and ophthalmic cortisone of definite value. A word of caution is warranted, particularly with reference to the use of local anesthetics as a number of patients develop definite allergic reactions to the local anesthetic ophthalmic drugs. Many of these patients have had repeated attacks and have developed previous sensitivities to exposure. The discovery of the allergen, desensitization and an avoidence program are advisable.

Thomas and Warren [11] in their "Analysis of Thirty Consecutive Cases of Allergic Conjunctivitis," found that only six of the thirty patients, or

20 per cent, had no other allergic manifestations. Fourteen of the thirty cases revealed that skin tests substantiated the patient's suspicion of certain aggravating inhalants. The patients were observed over periods of from two months to four years and eight months. The results of treatment were classed as good, fair, poor and no report—not treated. It was thought that 50 per cent of the patients handled showed a satisfactory response to treatment. This group of patients were not selected but consisted of thirty consecutive cases of allergic conjunctivitis with no exceptions.

(b) *Phlyctenular conjunctivitis* is characterized by a small pinkish-white elevation which appears in the midst of the hyperemic area. A tiny gray crater develops at the apex and the rest of the conjunctiva is clear and unaltered.

(c) *Vernal conjunctivitis* is frequently recurrent, bilateral and an interstititial type of inflammation of the conjunctiva. It is frequently of a seasonal incidence and of as yet unknown etiology. It is characterized by flat-topped papules, usually on the tarsal conjunctiva, resembling cobble stones in appearance; by a gelatinous hypertrophy of the limbal conjunctiva, either discreet or confluent, accompanied by corneal involvement and associated with marked itching, redness of the eyes, lacrimation and the mucoid or lardaceous discharge usually containing eosinophiles. In addition to the palpebral involvement of vernal conjunctivitis, one not infrequently will notice a bulbar type of involvement. The most plausible explanation of vernal conjunctivitis is that of a conjunctival manifestation of allergy, the irritating agent most frequently being dust. It may be aggravated by dry heat and it occurs frequently in vagotonic types of individuals. This postulated etiology resembles that of phlyctenular conjunctivitis, but whereas the latter is an endogenous bacterial intoxication, the former is exogenous and not bacterial.

(d) *Corneal Involvement*

Allergic manifestations of the cornea may be classified as follows:

(1) *Superficial punctate keratitis*—The allergic etiology is characterized by multiple tiny ulcers in the epithelial layer of the cornea which stain with fluorescein. Pain, lacrimation and photophobia are symptoms and these disappear rapidly on avoidance of contact with the offending agent. For example, if the agent were shaving cream the dermatitis might disappear several hours after shaving, occurring only in the morning. Often the patient discovers the offending agent and symptoms are controlled by avoidance. In chronic forms the dermatitis often proves to be refractory to treatment, and the offending allergen is difficult to discover. It is remarkable how rapidly many of the patients presenting superficial punctate keratitis will respond to the local use of an ophthalmic solution of Cortone.®

(2) *Kerato-conjunctivitis* may be further subdivided into three distinct types. The first type, or simple inflammatory ulceration of the cornea with associated inflammation of the conjunctiva, is very common. The conjunctival vessels stand out prominently and there is general inflammation and redness with some lacrimation and photophobia. The cornea, when stained, usually shows ulceration. In chronic or longstanding cases, there may be a progressive vascularization of the superficial and deep layers of the cornea stimulated by re-exposure to the allergen, as well as scarring or tissue overgrowth not present in the early cases. The eczematous keratitis of infants is of this type. According to Ruedemann[6] the incidence of kerato-conjunctivitis is nine times as great as that of keratitis, although the course and treatment are similar.

(3) *Phlyctenular kerato-conjunctivitis* is rather infrequent. It was formerly thought to be due primarily to tuberculosis; however, the lesions have been found to be caused by an exudate of leukocytes in the bulba or corneal conjunctiva. Lesions of an allergic nature are usually of the atopic type; and I have observed similar lesions in a patient with a definite mold sensitivity. The adjacent conjunctival vessels at the limbus dilate when the cornea is involved, causing a superficial corneal vascularization. A limbal phlycten may extend toward the essential area of the cornea. The peripheral area of the ulcer heals, but the central margin remains active. The ulcer remains superficial and never perforates. The fan-shaped, superficial opacity, densest where the ulcer has stopped, remains permanently.

(4) *Marginal kerato-conjunctivitis* may be distinguished from the other types of kerato-conjunctivitis because it is characterized from the onset by pin-point ulcers along the margin of the cornea with symptoms of pain, photophobia and lacrimation. These are beautifully brought out when stained with fluorescein. A crescent-shaped ulcer is formed by the coalescence of small lesions. An area of clear cornea remains at the limbus, and on the adjacent bulba conjunctiva there is a small area of edema. If the lesion progresses the vessels may appear to cross the limbus, and infiltration of the cornea may stand out toward the center of the marginal ulcer. Clinical evidence of vitamin deficiency should be considered or ruled out in this type of conjunctivitis since such a deficiency may coexist with the presence of an allergy. The scars following these ulcers which have coalesced at times range from a slight greying of the cornea nebulae to a thick heavy scum or leukoma which produces economic blindness. Many times if these patients are caught early, particularly if one can elicit the etiologic agent and institute local treatment in a matter of hours, employing such therapy as Holocaine® and epinephrine, or with the use of Cortone®, symptoms may be absolutely controlled without any residual scar formation. One may be able to reproduce at will ulcers and desquamation following re-exposure to such an offending agent, for example, face powder containing orris root. One must be very careful in

the treatment of these patients, not to use atropine if there is any evidence or history of atropine sensitivity. It is usually better to use scopolamine or omit dilatation rather than to increase the corneal edema.

(5) *Corneal Infiltration* is due to one of the above lesions and may be superficial or deep. A sensitized cornea may react to an offending allergen, as producing a definite vascularization with secondary scarring confined to the superficial layers of the cornea. In the deep or profunda type, or dermatitis profunda, the interstitial keratitis is not infrequently associated with an anterior and usually unilateral uveitis. It is similar in most respects to the infiltration encountered in tuberculosis, congenital syphilis, leprosy and undulant fever. This is the allergic reaction to a mild chronic infection. It occurs in patients with impaired resistance, and is sometimes precipitated by an intercurrent, acute respiratory infection, or even trauma. In tubercular interstitial keratitis, the allergic reaction to the toxins of tubercle bacillae produces an infiltration of a nodular type and localization, vascularization in the middle and deep layers of the cornea, frequently limited to a sector only. The disease is often unilateral. Fine and Sweeney[4] have reported a case of seasonal allergic iritis in some detail and reference is made to a definite seasonal allergic etiology which was present over a period of twelve years. A careful review of the literature, classification and essential diagnosis were discussed by these authors and the results of treatment by Cortone® acetate suspension and desensitization with a non-bacterial antigen was reported. The case further showed that non-bacterial antigen allergens must be considered as an etiologic factor in the production of iritis of unknown etiology.

(6) *Corneal dystrophies* include the dusty, edematous corneal epithelium frequently seen in vernal catarrh and keratoconus. These lesions may be produced in the absence of an allergic reaction in normal ocular tissues. Although this is thought to be related to the poor nutrition of the cornea, which may result from an allergic reaction in the bulbar conjunctiva or an interference occurring at the surface of the superficial cell layer, the relation of calcium deficiency to these lesions is not well substantiated, and it is believed that most of them have an allergic basis. A very rare corneal dystrophy (Salzmann's dystrophy) that occurs in occasional cases, does follow phlyctenular keratitis and is characterized by a bluish-white nodule in the superficial cornea, most frequently situated near the edge of the pannus. They may cause visual loss with irritation phenomena, but according to Duke-Elder[3] the latter may be present intermittently in acute attacks.

Thomas and House[10] reviewed thirty-five cases of corneal allergy of which twenty-three had detailed follow-up. It was found that the lesions in these cases were divided into six types, as follows: (1) superficial punctate keratitis, (2) ulcerative kerato-conjunctivitis, (3) phlyctenular conjunctivitis, (4) marginal kerato-conjunctivitis, (5) superficial and deep corneal infiltration and (6) corneal dystrophies. The diagnosis of corneal allergy in these cases was considered. The incidence of tuberculosis in the

group was discussed. The result of treatment was good or excellent in eleven of the twenty-three treated, or 47 per cent. Improvement was noted in twenty of the twenty-three cases, or 87 per cent. These figures were found to compare with the results quoted by other authors in the management of allergic diseases.

3. *The Iris*

(a) *Benign iritis* is an intraocular involvement frequently associated with foods producing gastrointestinal disturbances. It is probably not as common as reactions to external irritants or pollen-food combinations, but these agents definitely produce iritis at times. Allergic iritis is a mild congestive condition without plastic exudate, less painful than the usual form of ocular allergy, which tends to develop and disappear rather rapidly. Undoubtedly there are many cases of iritis due to bacterial allergy. They may be associated with an infection of the prostate or other foci such as the tonsils, gall bladder or appendix. At times during an acute phase of iritis, desensitization may be instituted and one may note a subsidence of the acute symptoms. This is particularly true in those patients who have a pollen sensitivity. Since the advent of ophthalmic Cortone® acetate, these patients are offered a definite therapeutic adjunct of rapid type which we have sorely needed in past years, and which has facilitated the management of these patients a great deal.

4. *The Lens*

(a) *Myopia*—Many cases of myopia have been found to be associated with allergy and are accompanied by progressive changes. The patients with myopia, as reviewed by Ruedemann and Thomas[6] indicated that the incidence was much higher in the allergic group than in other ophthalmic cases. It was further noted that these patients may suffer a definite exacerbation of symptoms during the hay fever season. The author had the opportunity of following a case of progressive myopia in which a definite food sensitivity was determined and, following the elimination of peas in the diet, there was a definite arresting of the progression, and subsequently with a lax program, a further progression was noted.

(b) *Cataract*—The lens may be involved in an allergic process which produces either diffuse or disseminated lenticular opacities. Such changes are rather slow in their onset and one is able to note progressive clouding to develop which may be caused by food sensitivity. This type of involvement is frequently seen in young adults and may be seen in children or adolescents, particularly associated with an atopic dermatitis which is further evidence that the lens is epidermal in origin and one is able to further appreciate the correlation with an atopic dermatitis. Elimination of the etiologic agents does not always halt the progress of the changes in the lens, although apparently retards it in certain instances. There are many juvenile cataracts which may be successfully operated on, particularly

when they are related to an atopic dermatitis. I have seen several such patients who were economic hazards who have been satisfactorily rehabilitated following satisfactory cataract surgery.

5. *Vitreous Body*

(a) *Vitreous opacities* have not been at all uncommon in our cases of allergy and the incidence is thought to be definitely higher in these cases than in non-allergics. Progressive degeneration of the vitreous body warrants an allergy investigation. These opacities may range from a fine black dot to numerous heavy, mossy, vitreous opacities of the type frequently associated with tuberculosis. They are seen to float or drift across the visual field and may occur in varying degrees of severity. Some are only annoying to the patient, while others are definitely dangerous, clouding the medium and causing definite diminution of vision. Many times patients will come in with a complaint of a fixed black spot or note a moving obstacle across the visual field.

6. *The Retina*

(a) Retinal changes are divided into two general types: hemorrhage and retinal detachment. Retinal hemorrhages are thought by certain investigators to be a purpuric type of reaction associated with ocular allergy, and which may be explained on an allergic basis, or the consideration of an allergic purpura. I recall a patient who had a tar sensitivity to tar fumes who had a definite allergic purpura, accompanied by minute retinal hemorrhages along with a hematuria and other skin manifestations of purpura. Zussman's[12] patient was subject to recurrent migraine-like headaches and was found by the examining ophthalmologist to have fields of vision of both eyes that were markedly contracted for both white and color vision. The report presented four media charts showing the marked contraction of the visual fields which were followed over a period of five months. The authors were of the opinion that this was an unusual case of ocular allergy, wherein the picture of localized retinal edema was absent and was over-shadowed by a picture of mottling and pigmentation of the fundus periphery, together with a marked contraction of the visual fields.

I had the opportunity of seeing a patient with an allergic migraine who reported a definite impairment of vision and a partial blindness that was unilateral on the side of the headache. The fundus examination revealed a definite palor and edema of the nerve head, which was observed on several occasions during the acute period of pain, and after the headache subsided the fundus was normal.

Ocular allergy may be a more common cause of retinal detachment than has heretofore been suspected. It is thought that a wheeling reaction of the retina pushes off of the retina causing a detachment.

(b) *Retrobulbar neuritis* resulting from over indulgence in alcohol or tobacco is usually due to sensitivity to a special grain of alcohol or to a

particular type of tobacco or to a chemical used in the manufacture of the tobacco, and may be explained on the basis of increased capillary permeability, presumably wheal formation. There may be definite edema of the macula and nerve head. Involvement of the nerve between the eye and the optic chiasma develops and is usually classified as retrobulbar neuritis.

7. *The Orbit*

(a) *Muscle imbalance* is definitely aggravated or increased during exacerbations of a patient's allergic manifestations, particularly a rhinitis or a hay fever. One also may notice such an involvement in cases of migraine. On occasions, one is able to determine a slight exophthalmus occurring during allergic episodes, and which may produce a secondary muscle imbalance. Within the past two months, I saw a patient with a definite allergic rhinitis having an exophthalmus not related to the thyroid which was influenced by an allergen. On occasions, with an overdosage of extract, a definite increase of exophthalmus was noted by the patient which would decrease in a matter of hours.

TREATMENT

The treatment of ocular manifestations of allergy may be grouped as follows: (1) Local treatment, (2) Avoidance, (3) Dietary restrictions, (4) Hyposensitization, (5) Irradiation with Beta radium.

Local treatment should not be instituted by an allergist without the cooperation of a competent ophthalmologist. This is particularly important because a period of twenty-four hours of mismanagement may result in a permanent impairment or loss of vision, particularly in those cases having a definite corneal involvement. It is necessary to use vaso-constrictive drugs as well as local anesthetics; however, the physician must be cautious with these due to the many cases of sensitivity to drugs or ophthalmic ointments. Holocaine, Pontocaine and similar drugs are desirable if there is no sensitivity, but should there be a question, the patient should be patch tested before their use. A review by Theodore[7] is very timely and he emphasizes the fact that since drug irritation can be avoided by using properly prepared solutions of the same drug, drug allergy requires substitution of a different drug. It is of great importance at times to make a distinction between these two types of drug intolerance. In consideration of drug allergy, it is necessary to eliminate the offending medicament and to employ a drug of a similar pharmacological action, preferably a drug which is less likely to sensitize. The use of antihistamines in the eye have been beneficial in certain instances; however, one has to be cautious and determine a patient's intolerance to certain of these antihistamines. A review of this subject was considered by Hanns-Jurgen.[5] One must always keep in mind the fact that antihistamines may be a possible aggravating therapeutic agent when used locally in the eye. A brochure prepared by Merck and Company, Inc., Rahway, New Jersey, coprighted

1951, regarding the use of Cortone® in eye diseases is very timely. Cortone® has been a great asset in the handling of these problems and has prevented blindness and has shortened the period of disability in many patients having ocular conditions, particularly the inflammatory diseases of the eye. Only in cases of involvement of the deeper ocular structures is systemic administration of this drug required.

Eye pads are desirable, not only for protection, but also in the presence of photophobia. Other local treatment may be considered by the ophthalmologist depending upon the progress of the patient.

AVOIDANCE

Avoidance of nonspecific irritants of inhalants as well as chemical agents which either the patient or the doctor might suspect is highly desirable. Sensitization studies will reveal evidence of other inhalant sensitivities and the same type of avoidance program for patients suffering with allergic rhinitis and asthma should be followed in patients having an ocular allergy. It is extremely important that pillow covers or rubber pillows be used if there is any question of dust or feather sensitivity, or a sensitivity to molds which may accumulate in pillows. The effectiveness of this program is, of course, dependent upon the willingness of the patient to cooperate, as well as upon his ability to understand and carry out instructions.

DIETARY RESTRICTIONS

Dietary restrictions are based upon the results of sensitization studies, the experience of the physician and the suspicions of the patient that certain foods are more likely to cause trouble than others. In those instances of marked dietary restrictions, supplemental vitamins, preferably of the synthetic type, are warranted. Dietary restrictions should always be temporary, extending over a period of two to four weeks, and modified by a trial period of at least five days with a food. If a food is found to consistently cause distress, it should be eliminated for an indefinite period and the diet modified if any deficiency might result therefrom. By the elimination and addition of food to the diet, we are able, at times, to determine the true offenders.

IRRADIATION

Irradiation with the use of Beta radium is of controversial value; however, there are many instances in which either Beta radium or other types of radiation are of value, particularly in the handling of vernal catarrh and possibly other ocular lesions. I have seen it used in patients with corneal scarring as a definite adjunct in the management of these patients, not only to control the tissue over-growth, but also to offer the patient comfort, and there have been certain instances in which the lesions have been found to disappear entirely after this type of treatment.

COMMENT

Consideration of allergy as an etiologic factor in certain diseases of the eye and adjacent tissues has contributed much to our knowledge of the management of conditions which were formerly not controlled, although they were treated vigorously with non-allergic methods. It is felt that ocular conditions which do not respond to conventional management should certainly be given a careful trial on an allergy program. A diagnosis of an allergic factor in these conditions is frequently supported by other allergic manifestations. Many of the tissue changes are characteristic in appearance. Significant reactions to sensitization studies are further evidence implicating an allergic factor. A patient with a positive family history of allergy warrants the consideration of an allergic investigation because of the seriousness of involvement and of the complications which may result from neglected cases. A therapeutic trial in management often shows results and, at times, we are able to reproduce lesions at will by recurrent exposure to the offending allergens.

SUMMARY

In summary, the question of ocular allergy may be considered through a therapeutic trial. If the treatment offers results, if the patient improves and if the reaction can be produced at will, the condition is usually allergic. Questionable cases should be given a therapeutic trial. Allergic involvement of the eye as a whole or tissues selected or adjacent are considered relative of allergy by the mechanism of smooth muscle spasm, increased capillary permeability and reactions of the reticulo-endothelial system. It is now recognized that the entire eyeball, as well as tissues in the socket, are capable of allergic reaction, and the extreme pain suffered by these patients, especially in allergic migraine, may be reflex or central bulba type of pain in character. Interference in nutrition of the cells or areas caused by this disturbance is the result of an allergic involvement caused by an altered blood supply to the eye. Such a disturbance explains illusions encountered in ulcerated phlyctenular kerato-conjunctivitis. The treatment of ocular manifestations of allergy has been grouped according to local therapy, avoidance, dietary restrictions, hyposensitization, irradiation. The importance of the close co-operation of the ophthalmologist and the allergist in a united approach cannot be over-emphasized.

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EHRLICH - VON BEHRING CELEBRATION

On March 13 to 16, 1954, under the sponsorship of the President of the Federal Republic, Professor Theodor Heuss, the 100th Recurrence of the birthdays of Paul Ehrlich and Emil von Behring will be celebrated in Frankfurt/Main and Marburg/Lahn. Both of these German research scientists were distinguished with the Nobel Prize. Paul Ehrlich, who was active in Frankfurt, invented Salvarsan in 1909. To Emil von Behring mankind owes gratitude for antidiphtheria and tetanus serum, and also for instituting serum treatment and protective vaccination against these two dreaded diseases. A Memorial Service will be held in the Paulskirche in Frankfurt/Main and during the Commemoration services the Paul Ehrlich Prize will be bestowed upon Dr. Ernst Boris Chain. Monday, March 15, an entourage will leave by special train for an academic celebration in the auditorium of the Phillipps University of Marburg/Lahn. There will be an address by the Rector and presentation of the Emil von Behring Prizes, addresses by the recipients of the prizes, dedication of the anniversary building of the Behring Firm and opening of the Emil von Behring Exhibition in the University Museum. On Tuesday, March 16, there will be a Scientific Convention in Frankfurt-Hoechst on "New Discoveries and Problems in Chemotherapy, Immunobiology and Virus Research." There will be guided tours through the new Paul Ehrlich Research Laboratorium of the Farb-Factory Hoechst. Those planning to be in Europe at this time, and who wish to attend this celebration, should make requests for further information to: Sekretariat (Presse), Ehrlich-von Behring Celebration, Marburg/Lahn, Universitaetsstrasse 7, Landgrafenhaus.

THE ASTHMOGENIC EFFECT OF ODORS, SMELLS AND FUMES

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A SEARCH of the literature demonstrates the fact that the effect of odors and fumes on asthmatic patients is either the most neglected or else the least publicized aspect of the subject. This appears to be true despite the general knowledge that behind the relatively few published observations lies a long and respectable history of osmyls as causing not only coryza and bronchospasm, but, as well, eczema and urticaria.

The ancient Greeks used perfumed headrests for the treatment of insomnia, the deep, slow respiration caused by the exposure to pleasant odors inducing sleep. Today we use pillows filled with pine needles and other aromatic substances for similar purposes. The Romans used burning feathers and smouldering leaves to stimulate respiration, a counterpart of the modern method of applying spirits of ammonia to the nostrils of fainting patients.

Mackenzie[14] in 1855, described "rose colds" as such. The textbooks usually teach that the patients are likely to blame roses, either because they appear most profusely at the peak of the grass pollen season or because the rose petals carry actual grass pollen grains, which the patient inhales. Roses free of pollen will, and do, cause coryza in susceptible patients. Urbach and Gottlieb[25] list the odors (not the pollens) of locust, pine and linden trees, of carnations, lilies, lilies of the valley, lilacs and violets, and also those of mock orange, privet and common elder, as causing coryza. In the patients studied, cutaneous and nasal insufflation tests with the respective pollens were completely negative. Urbach[24] has also described the smell of sage as causing symptoms. In 1937 Biederman[2] described similar responses to a number of flowers.

The smells of foods have been incriminated by a number of workers. In 1932, Feinberg and Aries[6] presented experimental work demonstrating both the particulate nature and the specific allergenic effects of the odors of peas, beans and lentils, and in 1937 Zohn[28] described similar reactions to the odors of spinach and peas. In 1940, Henson[10] described sensitivity to the odor of garlic, and in 1943 Sternberg and Sorrell[20] reported on nasal symptoms as caused by the fumes of coffee. In 1944, Horesh[11] described a patient whose asthma was induced by the odor of potato.

Cazort has, for many years, insisted that sensitivity to the odor of whole egg causes allergic disorders.

Tobacco smoke, as causing asthma in nonsmokers, has been listed by a

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number of students in this field. Harkavy,[9] on the basis of a great deal of experimental work, feels that tobacco allergy is truly present. It has been postulated by Rosen[16] that this is probably due to the irritant effect of the tobacco, rather than a true allergy. Harkavy, however, mentions a child whose asthma only occurred when the father smoked his pipe, and who was otherwise free of symptoms, while Rosen and Levy[17] describe a second child, who not only suffered nasal, ocular, pharyngeal and pulmonary symptoms, but also demonstrated tests positive, by passive transfer, for tobacco. In this case the mother's smoking initiated the child's symptoms.

The problem of tobacco sensitivity and irritation requires a great deal more study. In our own experience, approximately 75 per cent of the patients, male or female, who smoke more than twenty cigarettes daily are in various degrees, bronchitic. Of these, approximately 2 to 4 per cent present wheezing, which is lessened, or disappears, with the cessation of smoking. It is almost impossible to determine whether irritation, infection secondary to tissue damage, non-passive expiration bronchospasm due to excessive coughing, or allergy to tobacco itself, is at fault. As an occupational hazard in tobacco workers, Szentivanyi *et al*[23] find it equally difficult to distinguish between toxic, mechanical damaging and allergic effects. He and his colleagues tested 260 workers in a tobacco plant. Of these, sixty-one were discovered to be allergic to tobacco. These complained of cephalalgic migraine, angina, and dermatoses due to handling tobacco. Two patients demonstrated rhinitis and asthma. Similar tests on 160 control patients elicited only two tests positive for tobacco extract. Schirren[18] feels that a diacetyl compound is the allergen present in tobacco smoke, wood smoke, and coffee aroma. Patients certainly have been proven as reacting to any one, two, or to all three.

In some cases of karaya gum sensitivity, the odors, or components accompanying the gum preparation, may cause symptoms, the tests to the gums occasionally being negative. On the other hand, however finely subdivided its particles may be, a spray containing gum arabic may cause symptoms, as described by Fowler,[7] who demonstrated printer's asthma as due to a spray fluid containing acacia.

The problem of bakers and flour mill workers is more complex, because of the multiplicity of allergens and odors present. In one study, Linko[13] examined 326 workers, of whom seventy-six showed either probable or certain allergy to flour. Nasal symptoms usually occurred within four to five hours of exposure, depending, as well, on the concentration of flour dust. In one patient, asthma was seen following one inhalation of flour on the stairs, actually before entering the factory room in which it was prepared. Of fifty patients given flour to smell, there was a nasal reaction in forty-three, a control test with potato flour not reacting.

In another study by Shronts[19] 4500 employes were studied over a period of three years. Of these, five presented nasal, and two pulmonary, symptoms. In another previous survey of 550 employes, seven cases of respira-

tory allergy were discovered, all of the patients having been employed eight or more years. It is significant that these do not include the patients known to be sensitive to pollens or molds. Among these, there was an associated limited tolerance for mill dusts.

Back in 1912 Sticker[21] described the odor of linseed oil as causing respiratory tract symptoms. As recently as 1944, Derbes and Englehardt[5] reported asthma (and urticaria) as due to the odor of fresh paint.

Without careful experiments, it is sometimes difficult to discover whether the smell (free of demonstrable protein) or of the protein, free of odor, causes the bronchospasm. In the work of Feinberg and Aries[6] mentioned above, the material gathered on plates gave positive skin tests, demonstrating that some odors consist, really, of fine dusts, extractable, and capable of eliciting true proteinate types of intracutaneous tests. With other odors, however, as of range oil, this is probably not possible. There are many examples of such differing types of reactions.

Berg[1] described workers who, when exposed to paraphenylenediamine and toluenediamine, suffered from sore throat and lung inflammation, as well as asthma, presumably due to toxic, not allergic, effects. Wagner,[26] has, however, labelled similar symptoms due to exposure to solvents, as being allergic by nature. Stokinger's[22] description of reactions to plastic Teflon, leaves no doubt that the finely divided material can act like metal fumes, producing a disorder resembling "metal fume fever." This sets in within twenty-four hours of exposure, and consists initially of sore throat and dry cough, accompanied or followed by chills and fever, with aches and pains of the muscles and joints. When heated to about 360° F., Teflon gives off a very fine sublimate thought to contain hydrogen fluoride, which may be the cause of the nose and throat irritation.

Wittich's[27] review of the allergenic effects of chemical and dust pollution on respiratory tract allergies should be consulted for its complete list of such substances used in industry. Gardiner's[8] review lists a large number of antigenic substances to which industrial workers are exposed, and also a number of differing types of odors, gases and fumes responsible for allergic respiratory symptoms.

How far afield one may be taken in investigations of this type is seen in Jamieson's[12] paper, describing asthma due to the odors of urine, feces, perspiration and cheese. The patient, by bottle inhalation tests, reacted to the ethereal sulfates, which are the malodorous end-products of protein metabolism.

There are undoubtedly many such instances in the background of allergy practice, which do not result in case reports submitted for publication. On the other hand, our private practice demonstrates these syndromes so frequently that the subject seems to require re-emphasis. In some patients, especially those who have had previous studies, many report that questions regarding the effect of fumes have never been asked. Many of the pub-

lished case reports make no mention, either affirmatively or negatively, of such reactions. It is true that few patients volunteer such information, sometimes because they are not specifically questioned, or else because they do not believe the obvious causal relationship to be true. More often, they suffer from varying degrees of anosmia. The medication which relieves their symptoms often restores their sense of smell, but at the same time prevents the occurrence of further symptoms, excepting under special circumstances.

Our first patient with bronchospasm unequivocably due to exposure to the fumes of range oil, and to nothing else, was seen approximately ten years ago. Since that time we have gathered data on two hundred patients in whom fumes, odors and smells cause major symptoms, which could be brought on by exposure and relieved by elimination, in some cases resulting in complete and lasting relief. The questionnaire (Fig. 1) was devised to

Questionnaire

THE EFFECTS OF ODORS, SMELLS, FUMES, AND DRUGS

NAME: ..... DATE: .....

ADDRESS: ..... OCCUPATION: .....

The answers to the following questions will help your physician discover whether any allergic disorders are caused entirely or in part by exposure to any fumes, smell, gas, odor or drug. The circumstances in which itching or burning of the eyes, itching or running nose, dryness or burning of the lips, coughing, wheezing, itching skin or hives (wheals) occur, should be noted by circling the pertinent number, writing in the symptom to the right of the question.

GASOLINE FUMES OR ODORS	Symptom
1. Riding in a car?	
2. Travelling behind another car?	
3. Standing over running engines?	
4. Riding in a motor boat?	
5. Being in a garage?	
6. Going into gasoline stations?	
7. Being near gasoline refineries?	
8. Being otherwise exposed to gasoline fumes?	
Any other? Which?	

OIL FUMES OR ODORS?	Symptom
1. Riding in a bus?	
2. Driving behind a bus or truck?	
3. Going into bus stations?	
4. Being near oil burning furnaces?	
5. Handling an outboard motor?	
Any other? Which?	

KEROSENE OR RANGE OIL FUMES?	Symptom
1. Odors of kerosene?	
2. Kerosene burning space heaters?	
3. Kerosene burning kitchen ranges?	
4. Kerosene burning lamps?	
Any other? Which?	

GAS FUMES OR ODORS	Symptom
1. Gas refrigerator?	
2. Escaping gas?	
3 Gas range?	
4. Gas burning furnace?	
5. Gas heaters?	
6. Bottled gas range?	
7. Bottled gas refrigerator?	
8. Bottled gas heater?	
Any other? Which?	

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Fig. 1

COAL FUMES OR ODORS? Sympton

1. Coal stove?
2. Coal range?
3. Coal burning furnace?
4. Coal smoke?
5. Railroad trains or stations?
6. Charcoal fumes?
7. Exposure to briquettes?

Any other? Which?

WOOD FUMES, SMOKE, OR ODORS Symptom

1. Burning wood?
2. Wood fireplace?
3. Burning brush?
4. Grass fires?
5. Rubbish fires?
6. Exposure to evergreens? Pine wood?

Any other? Which?

PAINT FUMES OR ODORS? Symptom

1. Fresh paint?
2. Drying agents (Terebene)?
3. Turpentine?
4. Paint thinners?
5. Shellac?
6. Varnish?
7. Lacquers?
8. Radiator Paint?

Any other? Which?

HOUSEHOLD FUMES OR ODORS Symptom

1. Cleaning fluids?
2. Shoe polish?
3. Bleaching fluids?
4. Starch solutions?
5. Soap flakes or powder? Which?
6. Detergents? Which?
7. Dry cleaned clothing?
8. Rug cleaners?
9. Lighter fluid?
10. Brass polish? Which?
11. Silver polish? Which?
12. Furniture polish? Which?
13. Window cleaning fluids?
14. Spot removers?
15. Floor wax? Which?
16. Glass wax?
17. Ironing wax?
18. Toilet bowl cleaners?
19. Toilet deodorants?
20. Kitchen deodorants (wick type)
21. Incense?
22. Insecticides? Which?
23. Moth balls?
24. Dry mop fluids?
25. Sweeping compounds?
26. Dusting wax?
27. Dance floor wax?
28. Bowling alley wax?
29. Lysol (or phenol) Fluid or soap?
30. Cedar chests (bags, chips or paint?)
31. Any anti-odor preparation?

Any other household substance? Which?

COSMETIC FUMES OR ODORS? Symptom

1. In a Beauty Parlor?
2. In a Barber Shop?
3. In a Drug Store?
4. In a warehouse?
5. Using pine bath or shampoo?
6. Using tar bath or shampoo?
7. Exposure to perfume or cologne?
8. Nail polish?
9. Lipstick?
10. Rouge?
11. Eyebrow pencil?
12. Mascara?
13. Hair tints, rinses or dyes?
14. Face or body powder? Which?
15. Hand or face lotion? Which?
16. Rubbing alcohol?
17. Deodorants?
18. Antiseptics?
19. Soaps (scented or colored)? Which?
20. Skin cleansing agents?
21. Hair tonics?
22. Shaving lotions?
23. Cold wave preparations? Which?
24. Permanent wave preparations?
25. Toothpaste or powder?
26. Mouth lotion?
27. Douches (when applicable)?

Fig. 1a.

OFFICE FUMES OR ODORS? Symptom

1. Newspapers?
2. Magazines?
3. Inks?
4. Carbon paper?
5. Typewriter ribbons?
6. Stencils?
7. Duplicating fluids or jellies?
8. Cellophane?
9. Scotch tape?
10. Industrial or factory fumes? Which?

Any other occupational odors? Which?

RUBBER FUMES OR ODORS? Symptom

1. Rubber gloves?
2. Rubber in clothing?
3. Hot water bottle?
4. Rubber mattress or pillows?
5. Rubber pads?
6. Rubber upholstery?
7. Adhesive tape?

Other rubber objects? Which?

PLASTICS? Symptom

1. Furniture covers?
2. Mattress covers?
3. Pillow covers?
4. Playing cards?
5. Spectacle frames?
6. Plastic dentures?
7. Cements?
8. Ornaments?

Other plastics? Which?

SYNTHETIC FIBERS AND FABRICS? Symptom

1. Nylon?
2. Dacron?
3. Orlon?
4. Rayon?
5. Cellulose acetate?

DYES IN FOOD OR CLOTHING? Symptom

1. Artificial flavors? Which?
2. Artificial colors? Which?
3. Maraschino cherries?
4. Mint sauce?
5. Ketchup?
6. Soft drinks?
7. Colored liquors? Which?
8. Oleomargarine?
9. Butter (Brand)?
10. Dyed oranges?
11. Home dyes? Which?
12. Dyed clothing?
13. Dyed shoes?

Any other color or flavor? Which?

MISCELLANEOUS FUMES OR ODORS? Symptom

1. Tar fumes?
2. Asphalt fumes?
3. Hobbies? Which?
4. Photographic materials?
5. Paints?
6. Crayons?
7. Chalk?
8. Tobacco smoke?

Any other? Which?

INSECTICIDES? Symptom

1. Pyrethrum?
2. Chlordane?
3. Lindane?
4. D. D. T.?
5. Vegetable or fruit sprays?

DRUGS (*Please Underline*) Symptom

Handling, or taking by mouth, injection, application or otherwise: Aspirin, Acetanilid, Acetophenetidin, Acriflavine, ACTH, Aminophylline, Amphetamine, Aminopyrine, Anaesthetics (local), Antihistaminic Agents, Aquaphor, Argyrol, Arsenic, Asthma Powders, Aureomycin, Barbiturates, Benzoic Acid, Benzoin, Bismuth Subnitrate, Boric Acid, Bromides, Bromsulphalein, Butazolidin, Butesin Picrate, Butyn, Cetrimide, Chloral Hydrate, Chloramine-T, Chloromycetin, Cinchophen, Cinnamon, Citronella, Cocaine, Codeine, Codeinone (dihydro), Cortisone, Decholin, Demerol, Derris Root, Dinitrophenol, Dimercaprol (BAL), Diocaine, Diodoquin, Diodrast, Dionine, Emetine, Eosin, Ephedrine, Epinephrine, Ergotamine Tartrate, Estrogens, Floraquin, Formaldehyde, Furacin, Gantrisin, Gold, Heparin, Hydroquinone, Insulin, Intracaine, Iodides, Iodoacetic Acid, Isonicotinic Acid Hydrazid, Karaya Gum, Kwell, Larocaine, Liver Extracts, Mercurials, Morrhuate Sodium, Morphine, Para-aminosalicylic Acid, Parachlormetacresol, Parathion, Penicillin, Pentothal, Phenobarbital, Phenol, Phenolphthalein, Phenothiazine, Pontocaine, Privine, Procaine Amide, Seconal, Sedormid, Silver Picrate, Streptomycin, Sulfonamides, Terramycin, Tetmosol, Thephorin, Thiamine, Thiocyanate Potassium, Tyrothricin, Vioform.

Any other drug not listed? Which?

Any other substance, fume, odor or smell not listed? Which?

Fig. 1b.

help uncover other patients in whose illness the effects of osmyls might play a significant part.

The investigation into this aspect of the subject began as a series of oral questions directed towards the discovery of fume effects. It was obvious that, as uncovered by a first interview, such non-specific responses were comparatively rare. When, however, the questions were incorporated into a formal questionnaire which the patient and his family could study at home, affirmative answers occurred more frequently. The questions were listed as follows:

15. "Do you sneeze more in any special place? (Please underline) At home? At work? At school? At church? In crowds? At the mountains? At the seashore? In trains? On automobile trips? In museums? Libraries? Flower shows? Sport shows? County Fairs? At the circus? Department Stores? Any other places not listed? .....

16. If you sneeze more at home, is worse in any one room? .....Yes? No? Bedroom? Living room? Kitchen? Dining room? Bathroom? Cellar? Attic? Playroom? Barn? Kennels? Chicken coop? Any other place not listed?.....

21. Does handling any one thing(s) make you sneeze? Please describe.....

22. Is your sneezing worse with exposure to frying foods? Kerosene stoves? Fresh paint? Perfumes? Barber shops or beauty parlors? Tobacco smoke? Wood smoke? House dust? Hay? Grain? Animals (which)? ..... Cold air? Warm air? Steam?

23. Is your sneezing worse with eating of any food(s)? Which?.....

24. Is your sneezing worse with the taking of any medicines? Which?.....

49. Do you cough following exposure to fumes? Tobacco smoke?..... Wood smoke?..... Kerosene stoves or heaters?..... Frying foods? ..... Cooking smells?..... Fresh paint?..... House dust?..... Perfumes?..... Barber shops or beauty shops?..... Hay?..... Grain? ..... Animals (which)?..... Cold air?..... Warm air? ..... Steam?.....

64. Is the wheezing worse in any special place? (Please underline) At home? At work? At school? At church? In crowds? At the mountains? At the seashore? In trains? On automobile trips? In museums? Libraries? Flower shows? Sport shows? County fairs? Circus, On picnics? Theaters? Department stores? Any place not listed? Please describe.....

65. If the wheezing is worse at home, does it occur in any one room(s)? Bedroom? Living room? Kitchen? Dining room? Bathroom? Cellar? Attic? Play room? Barn? Kennels? Chicken coop? Any place not listed (Please describe)? .....

66. If it occurs at work, please describe occupation....."

As patients began to add fumes, odors or smells, or describe places where these were predominant, the list of substances the odors of which cause symptoms, began to grow. Careful investigation proved the conclusions previously recorded in the literature as fully warranted, and as occurring more frequently than was ordinarily suspected.

Impetus was given to these studies by a communication by Randolph[15] who, basing his hypotheses on specific sensitization to hydrocarbone and drugs derived from coal tar, drew up a lengthy list of substances chemi-

cally related, and capable of causing symptoms. It had previously been noted that a number of ethereal oils causing such difficulties were derivatives of terpene. Some, however, such as indole, skatole, and mustard oil, as well as anthralin acid esters, were nitrogenous in origin. Urbach and Gottlieb[25] list as well odors which do not clearly fall into either category, as, for instance, orris root, eucalyptus, camomile, and "aloes, valerian, parsley, hop, and dill," as well as "camphor, peppermint, and incense."

The incorporation into our original questionnaire of that prepared by Randolph,[15] augmented by such agents as had otherwise been reported in medical literature, resulted in the form which we now use. To this, for investigative and statistical purposes, we added a list of drugs to which reactions are known to occur.

It should be noted that approximately 85 per cent of asthmatic patients are not markedly affected by odors, fumes, smells, or drugs. Those who do report such effects as varying from slight annoyance to major symptoms, sometimes persisting for days, with freedom following change of environment or elimination of the odor, and exacerbation with re-exposure, require special study. The syndrome is as clear-cut as is any in the field of allergy.

In some patients there is only irritation of the nasal mucosa. In others, in addition, there may be sensations of laryngeal constriction. When the fume or odor is strong, or met with suddenly, there is a gasping expiration, followed by wheezing so immediate it must be seen to be believed. In those in whom the exposure is moderate and fairly discontinuous, the onset of symptoms may be insidious, consisting at first of the production of excess mucus by the membranes of the respiratory tract. In more severely affected patients, there may be a chronic cough which progresses, in some patients, into a reflex type of bronchospasm, extremely resistant to treatment, especially when exposure is persistent.

Predisposition (whatever that may mean) evidently plays some part in the syndrome, because it may be noted that in some families, in which several members may be typically allergic to inhalants or foods, only one, perhaps, will respond adversely to fumes. It should also be remarked upon that specificity occurs, the patient responding to all of one type of odor, or to several groups of odors, others causing no difficulty. If such responses were entirely reflex, and due to mucosal, non-allergic sensitivity, any sharp or acrid smell should cause difficulty. This is not true. A patient who wheezes when exposed to wood smoke may have no other similar responses, and tolerate fresh paint with impunity. Patients sensitive to perfumes may have no difficulty with other equally pungent substances.

It has occurred to some observers that the syndrome described could be psychological in origin. Such premises, however entertaining and suggestive, are not borne out by experience, especially in infants, and also in adults with a first known exposure, as, for instance, to household ammonia, boiling vinegar in pickling processes, or solvents for plastic cement. In some cases, as in pyrethrum sensitivity, or in symptoms due to factory

exhausts, as in the preparation of cereal foods, actual particles of the causative allergen are responsible factors, and positive skin tests prove the odor to be as particulate as a pollen. In others, dilutions of essential oils or osmyls so attenuated as to be barely noticeable, may cause immediate and alarming symptoms. With these patients, skin tests are negative. When skin tests are indicated and not done, or when the history is incomplete, such patients are often mislabelled as "intrinsically asthmatic" and sent to new geographical environments, in which they frequently, for obvious reasons, improve. As noted above, for purposes of record, they would perhaps better be termed "reflexly or nasogenically asthmatic."

The results of distributing the questionnaire can be seen in the following case reports, as drawn up from a list of fifty successive patients seen in private practice. Of these, seven only reported fumes, smells, odors or drugs as causing symptoms. Six of the seven had previously been studied, and in no case had this important aspect of the illness been uncovered.

In all of the patients studied, the following routine procedures were done: a complete personal and familial history, an environmental survey, a food check list, a psychosomatic evaluation, and pulmonary function studies, as well as the questionnaire for the effects of nonspecific factors and drug allergy. The laboratory studies included urine analysis, complete blood count, sedimentation rate, serology, and skin tests by pressure puncture and intradermal methods. In all asthmatic patients, x-rays of the chest and sinuses were studied. All those over fifty years of age had electrocardiograms. In a few patients, additional procedures were ordered as needed. The following case reports list only the pertinent allergic histories and the positive findings, and in addition, the answers to the questionnaire submitted.

Case 1.—L. B., male, aged thirty-two, suffered from nasal stenosis and rare sneezing attacks, with no coryza, no palatal or aural symptoms. Occasionally, he had tracheitis, with postnasal drip, developing to cough and wheeze, requiring no treatment excepting change of environment. The symptoms began two years ago, following a massive exposure to dimethyl sulfide, which caused severe nasal effects. There is a known sensitivity to house dust. The patient has suffered exacerbations with exposure to solvents. Antihistaminic agents, actually and by clinical tests, cause an itchy nose and nasal stenosis, with no relief of symptoms. There is a known sensitivity to aminophylline and to hydroquinone.

The patient's history demonstrates that symptoms as initially caused by exposure to house dust, became severe following an overwhelming exposure to the fumes of dimethyl sulfide in a manufacturing process. With a change of environment, the disorder cleared; with re-exposure, it re-occurred.

Case 2.—M. C., female, aged fifty, has had hay fever and bronchial asthma, with known sensitivity to grass and ragweed pollens and house dust. No relief has been found with ordinary antispasmodic agents or potassium iodide, but she has had good results with Cortisone. Skin tests have shown marked reactions to the tree, grass and ragweed pollens, and feather dander.

The patient's questionnaire reports attacks occurring in church, with exposure to

perfume, cooking smells, frying foods, and riding in an automobile causes coughing. Exposure to unlit cooking gas causes choking. Bleaching fluid odors and some soap powders "tighten the chest." Perfumes and deodorants bring on sneezing attacks. Hair tonics and shaving lotions irritate the mucous membrane, resulting in coryza.

Case 3.—M. H., female, aged twenty-five, has suffered from wheezing of eleven years' duration, perennial, with exacerbations in October, and with respiratory tract infections. There is known sensitivity to grass and ragweed pollens, the patient having had previous treatment with both, and also with house dust and mold extract.

The odor of kerosene causes coryza; exposure to fresh paint results in dizziness; soap powder causes prolonged sneezing attacks, with profuse coryza, and the patient has a known aspirin sensitivity.

Case 4.—J. D., female, aged nineteen, has suffered from nasal stenosis, cough and wheeze, perennial in nature, with exacerbations when exposed to house dust, cat and dog dander, hay and grain, with marked symptoms with change in temperature. Skin tests positive to all mammalian danders, house dust, and alternaria.

The patient's questionnaire showed that standing close to a running engine, or burning kerosene, causes epiphora; exposure to escaping gas causes bronchospasm, and wood smoke or tobacco smoke, causes burning of the eyes and a tight chest. Any ingredient of paint results in attacks of sneezing. Asthma occurs when exposed to cleaning fluids, shoe polish, soap flakes, lighter fluid, spot removers, furniture polish, fluid insecticides, and melting ironing wax. There is sneezing with the inhalation of the smells of sweeping compounds and cedar chests. Coryza occurs with proximity to freshly printed newspapers, and when changing typewriter ribbons. Adhesive tape causes contact dermatitis.

Case 5.—M. N., female, aged thirty-three, has had bronchial asthma of twenty years' duration, initially July to frost. It is now intermittently perennial, with exacerbations in September and October. There is known clinical sensitivity to feathers, house dust, grass and ragweed pollen, with positive tests to all four while other tests are negative.

The questionnaire elicits coal smoke from stoves or locomotives as causing wheezing. The patient has bronchospasm with exposure to any type of wood smoke. She wheezes with exposure to fresh paint. Sneezing follows exposure to bleaching fluids or Vel (detergent). Toilet deodorant (Red Cap) causes bronchospasm.

Case 6.—K. F., female, aged twenty-seven, has had hay fever and bronchial asthma each summer and fall, since she was thirteen years old. Previously studied, she has been treated with grass and ragweed pollen and house dust injections.

By questionnaire, the patient describes wheezing with exposure to burning brush fires, pine wood, fresh paint, turpentine, cedar chests, moth balls, perfumes, and the odor of plastic furniture covers (when new).

Case 7.—R. A., male, aged twenty-eight, has had nasal and pulmonary pollinosis, summer and fall types; typical stenosis, with coryza, epiphora, bronchospasm; with known sensitivities and positive tests to grass and ragweed pollens, pyrethrum, alternaria, and aspergilli. These have been relieved by Trimeton. The ingestion, extra-seasonally, of apple or apple cider causes immediate nasal and lung symptoms.

Wheezing also occurs with exposure to coal gas, coal smoke, fresh paint, floor wax, pyrethrum-containing insecticides, carbon paper, and asphalt fumes. Sneezing also is seen with exposure to perfume. Both sneezing and wheezing occur with exposure to Chlordane, Lindane, and D.D.T. Residual odors from weathered apples or windfalls cause immediate severe reactions of eyes, nose, throat, and lungs.

SUMMARY

Some of the nasal and pulmonary effects of odors, fumes and smells are described. A questionnaire which helps elicit the presence of such non-specific effects is presented.

It will be noted that the questionnaire has been copyrighted. This has been done only to prevent its commercial exploitation. It is not for sale. Any physician who wishes to use it in actual practice has only to request permission.

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AEROSOL TRYPSIN THERAPY IN THE TREATMENT OF ASTHMA

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FOLLOWING the report by Limber and his coworkers[1] on the use of crystalline trypsin (Tryptar)* by aerosol to promote the raising of purulent or viscid secretions from the bronchial tree, we have been interested in this type of therapy. The series of twenty cases reported by these authors reviewed for the most part patients suffering from bronchiectasis, tuberculosis, non-specific chronic bronchitis and unresolved pneumonia and pneumonitis; two patients with asthma were also included. The suggested rationale for the action of the product through its well-known digestive ability seemed quite logical to us. Furthermore, if trypsin could be shown to exert a proteolytic action on the tenacious, difficult to raise secretions, of asthmatic patients; and at the same time cause a minimum of irritation, it might readily become a valuable therapeutic agent in the management of bronchial asthma, particularly in the presence of primary or secondary bacterial infections.

SELECTION OF PATIENTS AND TECHNIQUE OF ADMINISTRATION

The seventeen cases reported in this study were selected from both private and clinic patients. Of this number, nine had primarily bronchial (atopic) asthma with secondary infectious complications, and eight were regarded as having primarily infectious asthma without significant skin tests to inhalant substances, and in whom food allergy could not be demonstrated. One patient of the secondarily infected type, and two with primarily infectious asthma had emphysema (Table I).

TABLE I

A. Bronchial (atopic) asthma with secondary infection (1 with emphysema)	9
B. Chronic asthmatic bronchitis (primarily infectious asthma) (2 with emphysema)	8

Following the procedure of Limber *et al,* we administered an antihistaminic preparation before the first treatment in each of our first two patients. After these first treatments were followed with no untoward manifestations whatever, and furthermore since antihistaminic preparations have been thought to retard the formation of bronchial secretions, which in this type of treatment would seem definitely undesirable, we discontinued antihistaminic medication in the remaining treatments of these first two patients of the series and in all additional patients. Instead, we routinely administered by aerosol 0.25 cc of 1:1000 aqueous epinephrine

*The Tryptar for this investigation was furnished by the Armour Laboratories.

before starting the Tryptar, on the assumption that it would not only counteract any irritating properties of Tryptar, but particularly in the hope that it would shrink the congested bronchial mucosa and permit the drug to reach more thoroughly into the bronchial tree.

Tryptar freshly dissolved in Sorensen's buffered phosphate solution was administered by "Pen-i-sol" aerosol apparatus employing oxygen for nebulization. At first we used the ordinary stock packages of Tryptar containing 250,000 units, dissolved in 8 cc of diluent, of which 2 cc (62,500 units) was employed for each treatment. It soon became apparent that our results were not as spectacular as those reported by the previous authors whereupon we increased the dosage first to 100,000 units and later to 125,000 units; in some treatments 250,000 units were used. However, we could see no advantage in using more than 125,000 units, and this amount was eventually selected as the routine dosage. Any solution which could not be used immediately was discarded inasmuch as the product is considered unstable after four hours. Ultimately, packages containing 125,000 units were available to us so that the entire amount from each vial could be utilized for each treatment without waste of any unused portions. Nasal cavities were irrigated with normal saline and patients were instructed to gargle with saline or water immediately after the procedure was completed.

Two patients received only one treatment and fifteen patients received treatments daily for one or more additional treatments, the greatest number of treatments being ten for one patient who received 1,250,000 units.

In all the patients of this series appropriate antibiotic therapy, symptomatic relief medication, expectorants, and conventional allergy management based on significant skin tests were carried out.

RESULTS OF TREATMENT

The results of aerosol treatments with Tryptar of the seventeen patients selected for this report are shown in Table II.

In one patient (E.R.) we felt that beneficial results were noted after the first two treatments. This twenty-nine-year-old woman suffering from severe and persisting chronic bronchitis as a complication of atopic asthma, was one of the first two patients we treated with Tryptar. She experienced no coughing throughout any of the treatments, but did complain of slight temporary nasal irritation. She mentioned that after her first treatment she experienced a sensation of "mucus moving about" in her chest; the next morning her sputum was raised more easily and there were fewer large lumps. She was given Tryptar by aerosol daily for an additional eight-day period, and after a lapse of two days took her final or tenth treatment. Throughout all this period she was receiving other treatment including antibiotics. Except for the questionable temporary improvement mentioned above we could see no definite sustained benefit either in lessening of the amount or increased liquefaction of the sputum.

Another interesting patient (M.C.), a forty-five-year-old woman with

TABLE II.

Case	Age	Diagnosis	No Treatment	Total Units	Results
B.G.	23	Chronic bronchitis Bronchial asthma	3	375,000 u	Sputum possibly raised more easily. Not increased in quantity.
C.M.	39	Chronic bronchitis Bronchial asthma	1	125,000 u	No change
F.M.	47	Chronic bronchitis Bronchial asthma Emphysema grade II	1	125,000 u	No benefit
A.H.	58	Chronic bronchitis Bronchial asthma	6	750,000 u	More sputum, but believe tryptar irritated. Burning in chest
L.E.	60	Chronic asthmatic bronchitis	2	250,000 u	Questionable increase in sputum
J.A.	25	Chronic asthmatic bronchitis	2	200,000 u	Severe asthma attack with each treatment
M.R.	67	Emphysema grade III Chronic asthmatic bronchitis	2	200,000 u	No change
E.R.	29	Chronic bronchitis Bronchial asthma	10	1,250,000 u	Increase in sputum at first. Ultimately no change
M.F.	55	Chronic bronchitis Bronchial asthma	6	750,000 u	No help
H.B.	52	Chronic asthmatic bronchitis	9	1,125,000 u	No help
L.P.	27	Bronchial asthma Chronic bronchitis	4	600,000 u	No help
T.H.	35	Bronchial asthma Unresolved pneumonitis	6	875,000 u	Questionable increase in lumpy sputum
D.H.	49	Chronic asthmatic bronchitis	3	375,000 u	Questionable temporary help
A.S.	37	Chronic asthmatic bronchitis	6	875,000 u	Colored sputum. Lumpy at first, then thin. Better
C.P.	34	Chronic asthmatic bronchitis Emphysema grade II	2	125,000 u	Questionable increase in sputum
M.C.	45	Bronchial asthma Chronic bronchitis	5	1,125,000 u	Sputum became thinner, then very lumpy, then gradually decreased. Some laryngeal irritation after last treatment
		2 months later	3	500,000 u	Much sputum, then better. Laryngeal irritation and swelling of eyes
		2 weeks later	1	125,000 u	Increased asthma 24 hours, then much cough, thin sputum and improvement. Hoarse for 12 hours. Refused further treatment
C.S.	20	Chronic asthmatic bronchitis	5	625,000 u	Sputum became lumpy after third treatment and raised more easily

chronic bronchitis complicating asthma caused by house dust, received 1,175,000 units divided into five treatments at daily intervals. After the second treatment her sputum became thinner, then quite lumpy and gradually decreased, but did not disappear altogether. She had some laryngeal irritation resulting in hoarseness after the last treatment. Two months later she experienced an increase in her infectious symptoms and was given an additional 500,000 units of Tryptar in three treatments at daily intervals. The sputum promptly increased in quantity, then lessened along with considerable improvement in her cough and wheezing. Following the first treatment in this series, she was somewhat nauseated and following the second she again experienced hoarseness for several hours. Two weeks later she was given one additional treatment of 125,000 units for another infectious exacerbation, following which she experienced a marked increase in her asthma for twenty-four hours until she raised a considerable amount of thin sputum, whereupon she was appreciably improved. This treatment, however, caused a very pronounced laryngeal irritation with

hoarseness lasting for twelve hours; she declined further Tryptar medication.

In another thirty-seven-year-old woman (A.S.) with chronic asthmatic bronchitis, who received 875,000 units of Tryptar divided in six treatments at daily intervals, we noted an immediate increase in lumpy sputum which later became quite thin and gradually decreased. She was regarded as improved by the treatment.

Our experience with one patient (C.S.), a twenty-year-old woman with primary infectious asthma, may be presented in some detail as an example of the difficulty in evaluating improvement following Tryptar administration to patients in this series. This woman, who had perennial asthma on an infectious basis since the age of two years, was hospitalized and started on penicillin, erythromycin and, as needed, intravenous aminophylline; she was continued on potassium iodide which she had already been taking for several months. The next day she was given intravenously 50,000,000 organisms of mixed typhoid vaccine, which caused a febrile response persisting for three days. Tryptar was started on the third hospital day while reaction to the typhoid vaccine was persisting. No change was noted in the character of the sputum from the first two treatments with Tryptar, but following the third treatment the sputum became very definitely lumpy and was quite easily raised. She was given two more treatments of Tryptar and was dismissed on the tenth hospital day, completely clear of her symptoms. We would like to attribute improvement to the Tryptar medication, particularly in view of the change in the character of the sputum following the third treatment. On the other hand, in our experience non-specific shock therapy such as resulting from the intravenous typhoid vaccine quite frequently is followed with spectacular improvement, as was noted in this case.

Of the remaining patients, five received questionable or temporary improvement only, and in six patients no symptomatic benefit or gross changes in the sputum of any character could be appreciated. One patient suffered a pronounced increase in asthmatic symptoms with each of two treatments of 100,000 units of Tryptar, and one other patient was questionably irritated by the medication.

DISCUSSION

We did not employ Tryptar in any case of strictly atopic asthma for the simple reason that the management of that type of patient has not presented too great a clinical problem in our practice. In infectious conditions, on the other hand, either complicating pre-existing asthma or producing asthmatic symptoms as a result of the infection, the need for an agent which would facilitate the raising of sputum is quite apparent. Furthermore, it often happens that patients who need them most cannot, because of idiosyncrasies, tolerate iodides, ordinarily our most reliable pharmacological expectorants.

Our overall impression of the use of Tryptar by aerosol to increase ex-

pectoration in asthmatic patients suffering from either primary or secondary bronchitis was one of disappointment. Of the seventeen patients receiving a total of seventy-two aerosol treatments with Tryptar in dosage varying from 62,500 to 250,000 units, only two obtained clear-cut beneficial results and five were questionably benefited. Furthermore, asthma was increased on two occasions in one patient, and laryngeal irritation was a repeated complaint following each treatment of another.

For practical purposes, we regard bacterial infection as frequently allergenic in allergic persons. On this premise it is understandable in the first place that Tryptar employed in our series might be expected to afford only temporary cleansing of the bronchial tree inasmuch as the infecting agent obviously would not be eradicated by the treatment and the mucopurulent exudate would continue to be produced. We have not tried Tryptar in patients suffering only with bronchitis without coexisting asthma. We should imagine that the product would offer more therapeutic aid in such patients than in allergic individuals.

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Medical Arts Bldg.

AMERICAN ACADEMY OF ALLERGY

There was a well attended meeting of the Tenth Annual Convention of the American Academy of Allergy at Houston, Texas, February 1-3, 1954, preceded by a two day Postgraduate course. All of these meetings were held in the headquarters hotel, The Shamrock. The scientific program was well chosen and well attended. There was a joint meeting of the Board of Trustees of the American Foundation for Allergic Diseases of the American Academy of Allergy and the American College of Allergists. There was also a meeting of the Joint Committee on Certification of the Academy and the College.

THE PROPHYLAXIS OF ALLERGIC DISEASE AND SOME FACTORS IN THE MANAGEMENT OF CHRONIC ALLERGIC DISEASE IN PEDIATRIC PRACTICE

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IN 1931 Rowe[30] made the statement that allergy, next to infection, is probably the most important single etiologic agent in human symptomatology. There has been no evidence in the years which have since elapsed to contradict this observation which, if true, emphasizes the importance of developing prophylactic measures against allergic diseases. Since most allergic disorders begin in childhood, prophylaxis, which is the ideal form of therapy, is the particular province of those dealing with children. We are only now, through studies of the hypothalamus-pituitary-adrenal axis, beginning to get leads in a direction which may ultimately reveal the fundamental constitutional abnormality which renders an individual susceptible to allergic disease. Until this is known, although perhaps not even then, a completely satisfactory or even rational program for the prophylaxis of allergic disease cannot be advanced. Nevertheless, certain facts are known and theories have been brought forward which deserve consideration in the study of this problem.

Although there had been many scattered references to various phases of the possible prophylaxis of allergic disease, the first paper devoted exclusively to this subject was published by Peshkin[23] in 1930, who specifically referred to bronchial asthma. The first publication on the general subject of the prophylaxis of allergic disease was written by Glaser and Landau[11] in 1936, followed in 1938 by a comprehensive discussion by Ratner.[24] The subject has since been reviewed by a number of others.[18,21,33]

It is generally accepted by most investigators, with Ratner[28] a notable exception, that the tendency to suffer from allergic disease is inherited. If this is the case, although it is impractical to urge that individuals with allergic disease should not intermarry, it should, nevertheless, be pointed out that such a marriage carries with it certain risks. Naturally, this does not always mean that one or more of the offspring will suffer from severe allergic disease. The offspring may not present any allergic tendencies or may merely demonstrate a transient atopic dermatitis (eczema) or a mild pollinosis. On the other hand, no physician can fail to be impressed by the tragedy of a situation in which one or both of the parents may be disabled by asthma, for example, and all of the children afflicted with severe forms of this or other allergic diseases. The suffering involved, and

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the economic and psychic strain placed upon the family, may be very real and very serious.

Every human being, and probably every animal, is, in all probability potentially allergic in that under certain conditions of health and environment, allergic sensitivity may be acquired. However, if we accept the concept that heredity is an important element in the development of allergy, we may then consider that for purposes of prophylaxis a potentially allergic child may be defined as one who has one or more allergic parents or siblings.[9] A recent study[20] in my practice revealed the astonishing fact that approximately 60 per cent of such children developed major allergic disorders before they reached the age of ten years. This, in itself, argues strongly for a hereditary factor in allergy since even without detailed statistical studies it is obvious that 60 per cent of the average pediatrician's practice does not consist of major allergic disease.

It is not the purpose of this discussion to indicate fully all the pitfalls involved in the study of heredity in allergy. I should only like to point out that certain important allergic diseases of infants and children, such as colic (in those instances where its allergic origin can actually be proved); the recurrent upper respiratory infections secondary to allergic nasal mucous membranes; perennial allergic rhinitis and migraine in childhood of proved allergic origin may be frequently forgotten when the histories of older children and adults are taken. This is true even if these conditions had been actually diagnosed properly, which in many instances is not the case. This, to a great degree, negates the value of the history in studies of heredity. It is only when children are carefully observed from birth by a physician trained in allergy, that the true incidence can be determined. Some allergic diseases particularly characteristic of children occur much more frequently than is generally realized. For example, in a study[20] of 516 allergic patients seen in my practice, ten years of age or less when first seen, recurrent upper respiratory infections on an allergic basis occurred in 30 per cent and perennial allergic rhinitis in 28 per cent. There are certain compensating mechanisms which tend to correct errors in computing the frequency of allergic diseases from the history alone. The two foregoing diseases frequently co-exist, and many allergic diseases of infancy and childhood are followed by other allergic diseases as the child grows older. For example, 42 per cent of the children in our series with recurrent upper respiratory infections on an allergic basis and perennial allergic rhinitis, subsequently developed asthma or some other major allergic disease.

Another compensating mechanism is that in the past atopic dermatitis (eczema) and seborrheic dermatitis (which is not an allergic disease) have not been sharply differentiated. However, one would hesitate to say that the present published studies of heredity in allergic disease are probably accurate because the errors of computing their incidence are subject to correction in the right direction because of these compensating factors.

Assuming that one or more of the parents or siblings in a given family may be allergic, the next point to consider is whether any form of management of the pregnant mother may help prevent allergy in the offspring. Ratner,[24] on the basis of certain experimental observations, felt justified in explaining allergic phenomena due to specific foods occurring in some children early in life as caused by over-indulgence by the mother in those particular foods during pregnancy. He believed that this sensitized the infant *in utero* and reported a series of cases in this category. In a discussion of another presentation on this subject by Ratner and Greenburgh,[26] Huber mentioned the striking instance of an infant whose mother ate peanuts in large quantities during her pregnancy. The child was never breast fed and within a short time after birth gave marked skin reactions when touched with peanuts, an observation strongly confirmatory of Ratner's thesis.

Ratner's views on this subject have, however, been largely discounted because it has been repeatedly demonstrated that reagins which can be verified by skin testing do not pass the human placental barrier. However, despite all evidence to the contrary it is impossible to avoid the conclusion of Ratner and others that the human infant may be born sensitized to specific allergens. It seems likely that this is due to *active* sensitization of the fetus *in utero* rather than an inherited specific defect of the germ plasm with respect to a particular allergen. In other words, it is probable that what is actually inherited is the *capacity* to become sensitized; not specific sensitivity to an individual allergen. Hill and Sulzberger[15] have stated that 85 per cent of all infants under one year of age who give positive skin tests react to egg white. The infant may react to egg white although there is no history of having ingested egg. It is possible in some instances to explain such sensitivity on the basis of egg in the diet of the mother passing through to the infant in her breast milk. Sensitization by means of food odors (osmyls) is a remote theoretical possibility that, while deserving of consideration, has not as yet been demonstrated in this age group.

Our work[10] has indicated that congenital sensitivity to other foods may also occur. In one interesting family there were five children, all of whom were sensitive at birth to cow's milk. Two reacted with atopic dermatitis (eczema) and two with both atopic dermatitis and asthma. By contrast, in an effort to prevent allergy to cow's milk, the fifth and last sibling was placed on soy bean milk starting at birth. He was unable to tolerate cow's milk when it was first introduced into the diet at the age of eight months and could not tolerate cow's milk when its use was attempted at the age of six years.

In order to prevent or minimize sensitization of the fetus to important foodstuffs, Shannon[32] in 1922, recommended that as a general prophylactic measure, all pregnant mothers should be cautioned to eat a large variety of foods and only a small quantity of any individual article of diet, and

that eggs be restricted rather than forced in the diet of the mother. In my opinion, this is sound advice and the pregnant mothers of potentially allergic infants in my practice are directed to avoid eggs as such and foods consisting largely of egg. It is also recommended, and I am sure this will be regarded as rank heresy, that the mothers drink not more than a pint of milk a day, boiled for ten minutes, and also that they eat no cheese. They are instructed to make meats in variety their chief source of protein and to take added calcium and phosphorus to make up for what they do not get in milk. The same diet is given the mother in those rare instances where she can be persuaded to nurse her baby.

Having now brought our potentially allergic child into the world we must next consider the subsequent steps. Breast feeding is urged since Grulee and Sanford[12] (even without placing the nursing mothers on the modified diet just mentioned), have shown that the breast fed baby has seven times as many chances of escaping eczema as the bottle fed baby. If the mother will not or cannot nurse the baby an attempt is made to start the infant on soy bean milk. The basis for this procedure is highly interesting.

When I first started practice in 1929, it was the custom of many pediatricians to start infants on raw egg yolk at the age of three months. This method of feeding had recently been introduced because at that time there was very widespread interest in rickets and anemia in infants and egg yolk was believed to be a good agent for the prophylaxis of both. It was soon discovered, in the course of routine feeding of raw egg yolk to children three months of age, that many developed rashes or other evidence of intolerance and within a few years this practice was almost universally discontinued. Egg yolk subsequently was not introduced into the diet until the age of six to nine months when it was much better tolerated. *This observation suggested that during the interval between three months of age and six to nine months of age the infant developed some type of protection against allergy to egg.*

It was well known at that time, as a result of precipitin studies,[2,6] that egg white protein could pass unaltered into the blood stream through the intestinal barrier. Reactions to egg yolk, for all practical purposes, are reactions to the egg white contained in the yolk. It was at first thought that perhaps the immunity to egg protein acquired as the child grew older was due to some anatomical change which would no longer permit the passage of unaltered egg white. However, with the development of the passive transfer reaction it was shown[27,36,38,39] that the intestinal tract is permeable to unaltered egg white and other proteins at any age. It thus appears evident that the protection acquired by the infant against egg white as the child grows older is immunologic in nature.

As I became increasingly interested in allergy in infancy, it became increasingly evident that cow's milk was responsible for many disagreeable allergic phenomena, as has been so ably described by Clein.[4] In his

practice, which is the practice of the pediatric allergist, he estimates its incidence as high as one infant out of every fifteen or approximately 7 per cent. What it is in the practice of most pediatricians not majoring in allergy is not known, but I am sure it is much higher than is generally suspected. With the knowledge that infants within the relatively short period of three to six months could develop immunologic protection against such a potent allergen as egg white, the thought occurred that if they could be started on some other food than the traditional cow's milk during this period of physiologic immunologic immaturity, the symptoms of milk allergy might be avoided, minimized or even prevented. Consequently, the incidence of atopic dermatitis (eczema) and intestinal intolerance to cow's milk, which comprises two of the most exasperating syndromes with which those dealing with infants must contend, might be minimized or even prevented. That such a possibility existed was indicated by the work of Grulee and Sanford,[12] mentioned above, to the effect that seven times as many infants developed eczema on cow's milk as compared with infants fed breast milk. Breast milk, which is the human infant's only "natural" food, as contrasted with cow's milk which is a "natural" food, not for the human infant but for calves, at least during the first few months of life, would appear to be the ideal food on which to start feeding the newborn infant. However, breast milk is not commonly available and although at times can be purchased, is very expensive and these facts preclude its general use in the feeding of potentially allergic infants. It is also now well known that a variety of substances ingested by the nursing mother may pass into breast milk to cause allergic disturbances in the infant and it would be impossible, for example, to get a dependable supply of breast milk from wet nurses who did not include egg in their diet. It therefore became desirable to secure a substitute for breast milk which would be readily available and of reasonable cost. The milk of other mammals, as the goat, is not commonly satisfactory because the sensitization is commonly to the casein fraction, which is closely related chemically and immunologically in the mammals whose milk is commonly used for human food.

Hill and Stuart, [14] in 1929, had introduced the first practical commercially available preparation of soy bean milk for use in infant feeding.* The soy bean is the only member of the vegetable kingdom, as shown by Osborne and Mendel[22] in 1917, which contains all the amino acids necessary for the normal growth and development of the human infant. Their statement is accepted today, with certain reservations as yet unpublished by Albanese† which has to do particularly with a deficiency of methionine, an essential amino acid not yet discovered at the time Osborne and Mendel made their report. However, this objection, Albanese indicates, is more

*Sobee, manufactured by Mead, Johnson and Company, Evansville, Indiana.
†Personal communication to the author.

theoretical than real since this deficiency can be compensated by ingestion of additional soy bean above a theoretical minimum (about 4.2 Gm/Kg/24 hrs) which these infants do in the course of satisfying their normal appetites. In 1929 Tso,[37] a Chinese physician, had succeeded in raising one infant from birth to the age of six months on a substitute milk made from soy beans without the addition of any protein of animal origin. Not long after the publication of his report I began feeding newborn potentially allergic infants soy bean milk as their sole source of protein. With the exception of the single case described by Tso and five cases of Sternberg and Greenblatt[34] reported in 1951 and my own eighty-eight patients,[10] similar experiments have not been published. Sternberg and Greenblatt found that feeding soy bean milk starting at birth throughout the first three months of life had no effect on the growth and development and blood protein values of these infants. Other than breast milk and soy bean milk we have used only meat base milk[8] and this in only a few cases.

For feeding our infants the starting formula was usually one-third of a commercial soy bean milk preparation‡ and two-thirds water, which was gradually increased to equal parts soy bean milk and water as the infants became accustomed to the formula. Hill,[13] in commenting upon our work, while granting that if well tolerated soy bean milk will nourish an infant as well as cow's milk, has pointed out that soy bean formulae are likely to cause diarrhoea and irritation of the buttocks which in newborn infants may become matters of serious concern. Hill's warning is appropriate and timely. The feeding of the newborn should be undertaken only by those who are well trained in this respect. However, when diarrhea and/or sore buttocks appeared, we endeavored to treat this in the usual manner but if unsuccessful discontinued the soy bean preparation. This was, however, necessary in less than 15 per cent of our cases, and this includes those infants where intractable colic and emesis also appeared to be due to the soy bean feeding.

The results of this method of feeding, as far as the prophylaxis of allergic disease is concerned, far exceeded our expectations. It is *a priori* reasoning, of course, that if one does not feed cow's milk to an infant, allergy to cow's milk does not occur. Only 8 per cent of our experimental group developed eczema as compared with about 30 per cent of the control group, the eczema in this 8 per cent of the cases, of course, being due to other factors than cow's milk. In a few instances where there was a congenital sensitivity to cow's milk, the infants reacted when again fed cow's milk at an average age of six to nine months. In only one instance, however, was the milk sensitivity retained after further prolonged abstinence from cow's milk.

Hill,[13] again commenting upon our work, inferred that while withholding cow's milk from the diet the first few months of life, would logically

‡Mull-Soy, The Borden Company.

minimize or prevent the development of allergy to cow's milk, that this could not reasonably be expected to prevent subsequent sensitization to other allergens as the child grew older and his view certainly appears to be good common sense. However, previous studies[20] in my clinic on the incidence and progression of allergic disease in pediatric practice, had apparently confirmed the observation, previously made by many others, that once the allergic state is established it tends to be followed by the development of other allergic diseases. For this reason, we thought it would be interesting to see what happened to our patients as they grew older. Much to our surprise, we found that only about 15 per cent of our experimental group developed major allergic diseases before the age of ten years as compared with about 60 per cent of our control group. This finding was so astonishing that we felt our experimental group might well be weighted in the direction of a greater incidence of allergies than might occur by chance in a random sampling of potentially allergic children. The reason for this was, of course, that these infants were placed on the experimental regime because their siblings or others in the family had suffered from various allergic diseases. Consequently, a second control group was selected. From reviewing the histories of 4,710 children in 1,215 allergic families, 175 were selected to comprise the second control group of this study. These children were followed for the same number of years as their opposite members in the experimental group and had the same number of younger siblings with closely similar allergic histories. Their parents, also, had allergic histories closely resembling the histories of the parents of the children of the experimental group. Members of the sibling, as well as the non-related control group, were considered as having allergic disease only if their symptoms occurred by or before the present age of their counterparts in the experimental group. We feel it is highly significant that in this non-related control group 52 per cent of the children developed major allergic disease as compared with 64 per cent of the sibling control group, a truly remarkable close correlation. Thus there is approximately a fourfold incidence of allergy in potentially allergic children started on cow's milk from birth as compared with those started on soy bean milk. It must be emphasized that to be successful, this regime must be instituted from the moment of birth. To give a potentially allergic newborn infant a trial feeding of cow's milk ignores the basic premise of this procedure, namely that these children have an immunological immaturity in the first few months of life which makes them predisposed to become sensitized to the first foods which are introduced into the diet.

Based on the same general reasoning for starting potentially allergic infants on soy bean milk instead of cow's milk to avoid sensitizing the infants to cow's milk, I feel it unwise to start these infants on such an important food as wheat for the first cereal. The infant should be started on other cereals, as barley, oats, rice and corn, using these successively so as to give the infant as great a variety as possible, introducing wheat

when the infant is between nine and twelve months of age. Buckwheat (which is not a true cereal) should not be used because of its high sensitization potential. Mixed cereals offer no particular advantages for potentially allergic infants but can be used after the component cereals have been introduced into the diet. Sensitivity to fruits, vegetables and meats occurs much less readily but the same general principles apply. One should use as much variety as is practical. The potentially allergic infant should not be fed orange juice daily, despite its low antigenicity when free from seed and oil,[29] but a variety of biogenetically unrelated juices, the ascorbic acid deficiency of some of these being made up, when necessary, by the addition of ascorbic acid. Fish should not be added until the infant is at least a year of age and nuts not until much later. In this connection, because peanut butter is a favorite food for young children, it should be pointed out that the peanut is not a nut but a legume. Egg, when eventually added to the diet, preferably not before the age of one year, should be started gradually in the form of hard-boiled egg yolk, hard-boiled egg white being added if the yolk is well tolerated and later, if this agrees, egg cooked by other methods may be tried. Allergy to the vitamins most important in infancy is so rare that it need not be considered as far as the potentially allergic child is concerned, provided simple A and D preparations are used

It was pointed out by Hutinel[16] as long ago as 1908, and later by Schloss,[31] that following acute gastrointestinal episodes, probably due to the increased permeability of the bowel, infants and children may become sensitized to foods which they previously tolerated. In acute gastrointestinal disturbances and in their convalescence, therefore, a variety of cooked foods of low antigenicity should be used, especially in children with allergic tendencies.

There are also occasional instances reported of sensitization apparently acquired by over-indulgence in specific foods. Stuart and Farnham[35] mentioned the case of a man, who as a child drank a can of glue on a bet, and thereafter reacted on eating fish with severe allergic manifestations. Alvarez and Hinshaw[1] reported one man who in his student days ate at one sitting two pounds of dates left over from a fraternity party and thereby became highly sensitized to this food. Another became sensitized to milk by taking from four to six quarts a day during treatment for tuberculosis. After that small amounts produced nausea and diarrhea. Ratner[25] has warned that fad diets, which are usualy composed of a limited number of foods, and very often raw foods, may be a potential source of food sensitization.

The environment of the potentially allergic child deserves careful consideration. The bedroom should be designed so as to be as free from house dust as possible, and also free from cooking odors, tobacco smoke, cleaning fluid, moth balls, gasoline (as in a room over a garage) and other strong or irritating odors. An unusual instance illustrating the importance of environment in the acquisition of hypersensitiveness, is men-

tioned by Ratner[25] who reported the case of an infant whose bedroom window faced a stable and apparently as a result of this the infant acquired sensitivity to horse dander, with a crossed reaction to horse serum.

The furniture of the room is also important. Most of the better quality of crib mattresses are satisfactory since they have plastic dust-proof covers. As the child grows older and needs a larger mattress, sponge rubber is the ideal material for this as well as for the pillow. Both should be enclosed in dust proof casings. The bedding should be free from silk, wool, hair, feathers and kapok. Good blankets made from synthetic fibers are now available. Fortunately, most of the animal toys have imitation fur made of rayon plush, which is harmless, and are stuffed with a good grade of cotton relatively free from the seed, which is a very powerful allergen. There should be no fur or feather bearing pets, regardless of negative skin tests or the apparent harmlessness of these pets on clinical observation. Insecticides should be free from allergens, especially pyrethrum, which is closely related antigenically to ragweed.

The importance of immunizing all normal children routinely against diphtheria pertussis, tetanus and smallpox requires no comment. However, such protection is especially important in the case of potentially allergic or allergic children because the antitoxins used in the prevention or treatment of diphtheria and tetanus are occasionally followed by disagreeable reactions. Protection against whooping cough is of paramount importance because of the marked tendency of this disease to aggravate bronchial asthma or initiate bronchial asthma in allergic children who have had respiratory difficulties. Pertussis in such patients is best treated with human blood derivatives which are relatively non-antigenic. Potentially allergic or allergic children exposed to measles should be treated with immune globulin for the purpose of modifying the disease because of the tendency of pulmonary complications in such children to pave the way for asthma. If a child has not been protected against tetanus by means of toxoid, the bovine tetanus antitoxin[7] of Sharp and Dohme is available, but should not be used in milk or beef sensitive children. It is also important that the allergic child be protected from other members of the family who have either acute or chronic respiratory infections.[17]

It seems hardly necessary to mention that children with eczema should not be vaccinated against smallpox, and children without eczema should not be vaccinated in families where there are other children with this condition not yet protected by vaccination. The reason for this is that for a few days after vaccination, the virus of vaccina circulates in the blood and tends to localize in areas where the skin has been damaged. The virus is also secreted in the mucous of the nose and throat and if towels or bedding, et cetera., contaminated by such mucous, are used by an eczematous child who has not been vaccinated, a generalized vaccinia may be contracted. This may at times be a very severe, disfiguring disease, occasionally fatal.

Recent studies in my clinic[3] have indicated that allergy to drugs occurs at least eight times more frequently in allergic children than in non-allergic children and, that following aspirin, penicillin is the most common drug used in the practice of pediatrics. This is some kind of a commentary on present-day medicine, concerning which time will give the ultimate judgment. Fortunately, aspirin does not possess a high sensitization potential and only 1.9 per cent of non-allergic children had reactions to this drug as compared with 10 per cent of allergic children who gave reactions to penicillin. In no instances were these reactions considered dangerous as far as life is concerned. It also appears to be a matter of common observation that the more a given patient receives of penicillin, the more likely the patient is eventually to become sensitized to this antibiotic agent. It is, therefore, in the interests of good medicine not to use penicillin when other antibiotic substances or sulfonamide drugs will accomplish the same purpose. This past year it appeared to be the consensus of allergists in replying to a questionnaire on this subject[19] that no one antibiotic should be constantly used but that the physician should have some system of rotating the various antibiotics for successive illnesses thus diminishing the chances of sensitivity to any one individual antibiotic drug.

In conclusion, the training of the child for eventual self support must be considered, especially in the case of the child with chronic asthma. One study has been made of this subject. Flensborg[5] in Denmark, investigated 298 asthmatic patients and stated that 116 of these or about one-third, had chosen a special profession on account of their asthma. It must always be borne in mind that once a person suffers from asthma, even though apparently complete recovery is made, just as in the case of tuberculosis, he is always subject to the possibility of a relapse. This has been illustrated during the recent wars when many former child patients who had been discharged as "cured" developed asthma when exposed to the activities of life in the armed services.

There are certain occupations obviously unsuited for the asthmatic person. These involve manual labor and other forms of excessive physical activity as professional athletics, or the teaching of physical education; exposure to excessive dust, cold moisture, strong odors, high or low temperatures and sudden changes in temperature. Bakers may develop asthma from exposure to flour dust; farmers, as well as veterinarians and others exposed to animals are often sensitized to various epidermoids; beauty parlor operators are particularly prone to sensitizations from the various ingredients of cosmetics. It seems reasonable that asthmatic children should not, in taking up music, study wind instruments. The use of such instruments is difficult for dyspneic individuals and it is also probable that they increase the tendency to emphysema present in all asthmatics. It is of the utmost importance that the asthmatic child should be aided in the selection of a career in which, if asthma persists or recurs, the earning of a living will not be impossible.

SUMMARY

The intestinal tract during infancy, as well as in later life, is permeable to the passage of unaltered protein. However, in the first few months of life, unlike later, the infant appears to possess an immunologic immaturity which favors the development of allergic sensitization to such foods as cow's milk and egg and probably other foods, though less readily. It was found that by feeding the newborn infant a substitute formula for cow's milk (soy bean milk), that not only was the development of allergy to cow's milk largely prevented in early infancy, but also that infants so fed developed approximately only one quarter as many allergic diseases in later infancy and childhood as infants started from birth on cow's milk formula.

Other suggestions are given directed at the prophylaxis of allergic disease and the management of chronic allergic disease in infancy and childhood.

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A NEW ALLERGY SYRINGE FOR TESTING AND TREATMENT

A new Allergy syringe has been announced by S. A. Axelrad of the Allergists Supply Company, 458 Broadway, New York City 13. The objectionable features of the Cooke syringe have been overcome by replacing the asbestos packing with a new inorganic rubber known as Corsol. The latter is nonabsorbent and does not affect extracts used by allergists, or other parenteral solutions. This new plunger is available with the Cooke allergy syringe. The Corsol packing is a tube on a threaded metal part. A slight turn to the right of the plunger in the barrel tightens the seal, while a slight turn to the left loosens the seal. This new syringe has been tested by many allergists with very favorable results. It can be sterilized in an autoclave or by wet sterilization. Another advantage is the low cost and interchange of parts.

THE USE OF BELLERGAL® IN THE PROPHYLACTIC TREATMENT OF SOME TYPES OF HEADACHE

CLARENCE H. STEELE, M.D.
Kansas City, Kansas

HEADACHE which recurs is one of the commonest presenting complaints encountered in the practice of medicine today. It has been estimated that six to ten million sufferers from headaches of the vascular type exist in the United States (according to Lennox[8]). Perhaps the actual number of persons afflicted with recurrent headache is much greater.

In spite of the voluminous literature on the subject of headache, with classifications and definitions of symptom-complexes, there is still much controversy as to the exact mechanism and origin of such headaches. Perhaps too much emphasis has been placed on attempting to classify headaches so as to have an orderly organization of the subject. Actually about the only constant factor in most headaches seems to be a vascular disturbance related to autonomic imbalance. Furthermore, as shown by Ogden,[10] persons with headache have a high incidence of respiratory symptoms and higher familial history of allergy. It is noted that these background factors frequently go along with emotional and occupational problems.

According to Wittich,[13] whether or not so-called migraine headaches are of allergic origin is not so important insofar as therapy is concerned, because most headaches are of the vascular type and are the result of dilatation of intracranial and extracranial arteries, together with an increased amplitude of pulsation of the vessels. The autonomic nervous system basically controls the action of these vessels. Vascular changes in the nasal mucosa and sinus mucosa, particularly at the sinus ostia in allergic disturbances, may cause headache of referred type as a result of pressure on the nasal endings of the trigeminal nerve, as shown by Wolff.[14]

Acute attacks of vascular headache can be controlled successfully in 80 to 90 per cent of patients with vasoconstrictor drugs, according to Horton,[5] Ryan,[11] Hansel,[2] and Hilsinger.[4] Ergotamine tartrate, dihydroergotamine (D.H.E. 45®) and ergotamine tartrate with caffeine (Cafergot®) are the drugs of choice. These preparations are effective in the acute attacks. Their use in the interval between episodes does not appear to reduce the frequency of headaches.

The emotional conflict and personality aspect of vascular headache have been stressed by Friedman.[1] Precipitating factors, such as tension, fatigue, worry, fear and anger, produce autonomic dysfunction and frequently act as "trigger" mechanisms in the initiation of headache. Therefore, prophylactic treatment directed toward regulating the autonomic nervous system,

Dr. Steele is an Associate Fellow of the American College of Allergists.

keeping to a minimum disturbing psychic influences and controlling allergic imbalances are beneficial in reducing the incidence of attacks.

The present study was undertaken to evaluate the efficacy of Bellergal* in the prophylactic and interval treatment of patients suffering from headache of varying type. The use of Bellergal (0.3 mg ergotamine tartrate; 0.1 mg bellafoline; 20 mg phenobarbital) for this purpose has been previously reported by Wittich,[13] Hilsinger,[4] Jones and Tod[6] and others,[3,7,9,12] have reported on its efficacy as an autonomic inhibitor. Ergotamine tartrate is a sympathetic inhibitor, bellafoline a parasympathetic inhibitor and phenobarbital a central and subcortical sedative. This combination of drugs apparently acts synergistically, having an inhibitory action on all three of the neurovegetative systems, thereby reducing the intensity of nerve response to stimulating experience. In a series of thirty-five patients who received Bellergal prophylactically for allergic, tension, histaminic or psychogenic headache, Wittich[13] reports 80 per cent of cases show good results, 11.4 per cent fair results, and 8.6 per cent poor results. Thirty of the thirty-five patients had allergic headaches, including mixed types. Hilsinger[4] after administering Bellergal to twenty-five patients with migraine, tension, or histaminic headache reported 68 per cent excellent results, 12 per cent good results, and 20 per cent poor results.

CLASSIFICATION

A group of forty-five patients suffering from recurrent headache was selected. Many of the patients (60 per cent) had headache of allergic type, including variants and combinations. Eleven patients, or 24.5 per cent, had migraine or "migraine equivalents" or "variants." In this group, the migraine feature predominated over the allergic or tension factors. Six patients, or 13.3 per cent, were diagnosed as having primarily tension headache. One patient had histaminic cephalalgia.

The average age of patients in the series was in the early fourth decade. Women predominated over men nearly three to one. As in several other reported studies, the group represented mostly allergic patients who had low tolerance to the commonly used vasoconstrictors. Many of them had been treated with a variety of procedures without satisfactory results. It was essential, therefore, to reduce the incidence and severity of headache and, in most cases, the patients were grateful for benefit received although recurrences of headache were not always stopped but merely lessened.

DOSAGE

The dosage of Bellergal was based on the clinical response of the patient to treatment, but was started at one tablet before each meal and at bedtime. As time progressed, treatment was reduced to the smallest effective daily amount as established by adjusting the dose in each case. The drug was withdrawn one week out of every four to six weeks in

*Sandoz Pharmaceuticals.

instances where prolonged treatment was necessary, in order to avoid the possibility of over-sedation. The average duration of therapy was fourteen weeks; the shortest interval was one week and the longest 104 weeks.

One patient experienced nausea to a degree which necessitated discontinuance of treatment after one week. This patient was highly unstable emotionally and it was believed that factors other than the drug might have been at fault. Other investigators reporting on the use of Bellergal have employed larger initial doses, that is, five to six tablets daily, in patients with emotional stress.

TABLE I.

Type of Headache	Number Patients	Results		
		Good	Fair	Not Relieved
Allergic (including mixed types)	27	10	9	8
Migraine	11	5	4	2
Tension	6	2	2	2
Histaminic cephalgia	1		1	
Totals	45	17	16	12
Results By Percentage		37.8	35.5	26.7
Satisfactory Results		73.3		—
Unsatisfactory Results		—		26.7

RESULTS

The results of interval and prophylactic therapy with Bellergal in forty-five patients suffering from a variety of types of headache are reported in this series. Classification of many of these headaches was difficult, but a careful study of the case histories, as well as observation of the patients and their responses to prior therapeutic measures served to place them in the categories in Table I. No attempt was made to discontinue or modify other forms of treatment in use at the beginning of the study.

Results of treatment were deemed good if the patient reported freedom from headache or only occasional headache of minor degree. Those who noted diminution in number and intensity of headache, and who thought they had received benefit from treatment, were classed as "fair results." Patients who received no benefit were classed as "not relieved." From the accompanying table it is noted that of the entire group, seventeen (37.8 per cent) showed good results, sixteen (35.5 per cent) had fair results and twelve (26.7 per cent) were not relieved. In the entire series, 73.3 per cent experienced "satisfactory results," that is, either were free of discomfort or had diminution in the number or intensity of headaches to a satisfactory extent.

Of the twenty-seven patients suffering primarily from allergic headache, including mixed types, there were ten whose results were good. Nine reported fair results and eight were not relieved. Nineteen (70 per cent) had either good or fair results and concluded that their treat-

ment was satisfactory. Some of the patients in the allergic group had cephalalgia of nasal origin, due in part to septal and turbinate deformities and in part to the usual edematous nasal mucosal changes typical of chronic perennial allergic rhinitis. It was frequently possible to relieve such patients during acute episodes of headache by cocainization of the nasal mucosa adjacent to the sphenopalatine or anterior ethmoid nerves. Such patients for the most part had septal deformities for which surgery was indicated. A large percentage of the eight patients in this group receiving poor results from treatment refused to have corrective septal surgery. It is believed that most of these would have been relieved had surgery been done.

In cases with allergic headache, concurrent therapy in the form of elimination of inhalant and ingestant allergens and hyposensitization was employed. Antihistaminic drugs were used only to aid in controlling flare-ups in allergic symptoms, and, in general, were avoided as a continuous form of treatment.

The eleven patients classified as having migraine were placed in this group after careful screening and, while a few showed elements of allergy or tension, these phases were of minor importance. The acute attacks of migraine were generally well controlled with vasoconstrictors such as dihydroergotamine (D.H.E. 45®) or Cafergot®. The latter preparation was used orally in some instances and rectally in others. Little difference in efficacy was apparent. Bellergal was used for the interval inhibition of autonomic activity in these patients. Five of them experienced good results, four fair results and two were not relieved. Of the eleven patients, nine (approximately 82 per cent) received benefit from this form of interval therapy.

There were six patients who were classed as having primarily tension headache. This number appears small when compared to the total number of cases in the series, but is not unusual in practice where a large number of patients seek relief from chronic nasal allergy. As reported by Wittich,[31] many allergic patients have a tendency to be nervous or psychoneurotic. They average more emotional trends and exhibit increased sensitivity to stimuli, with lowered thresholds to emotional strain. In this series, where cases have been placed in the group with tension headache, careful analysis indicated that tension was the major factor and the allergic state was of minor importance. Hence, the tension category is rather small.

Two-thirds of the patients having tension headaches showed satisfactory results from Bellergal therapy. In the two instances where patients failed to receive benefit, the personality and emotional conflict aspects were powerful and frequent. Rest and removal of undesirable stimuli were impossible to achieve. If it had been possible to institute psychotherapy for these persons, better relief probably would have been obtained.

A single patient with histaminic cephalalgia received fair results from

treatment. This number is too small to allow analysis. Histamine desensitization and nicotinic acid were used in this case, in addition.

SUMMARY AND CONCLUSIONS

Bellergal® in this small series, proved to have value in the prophylactic and interval treatment of a variety of headaches. The usual dosage was three tablets daily, except for withdrawal of treatment for one week out of every four to six weeks in instances of prolonged therapy. The average duration of treatment was fourteen weeks, with the longest interval being 104 weeks and the shortest one week.

It is difficult to evaluate the efficacy of a drug or form of therapy in the treatment of a clinical condition showing so many variations as headache. Of importance is the control of allergic states by elimination, avoidance and immunological methods. Personality features, feelings of insecurity, and emotional tension are present in some measure in most patients afflicted with headaches of the types under investigation. These factors must be controlled if possible, but at best resolution of such problems is imperfect. When utilized along with the aforementioned measures, the employment of a combination of drugs, ergotamine tartrate (sympathetic inhibitor), bellafoline (parasympathetic inhibitor) and phenobarbital (central and subcortical sedative), in this instance Bellergal, affords better therapeutic results than when attention is not given to the interval inhibition of increased autonomic activity.

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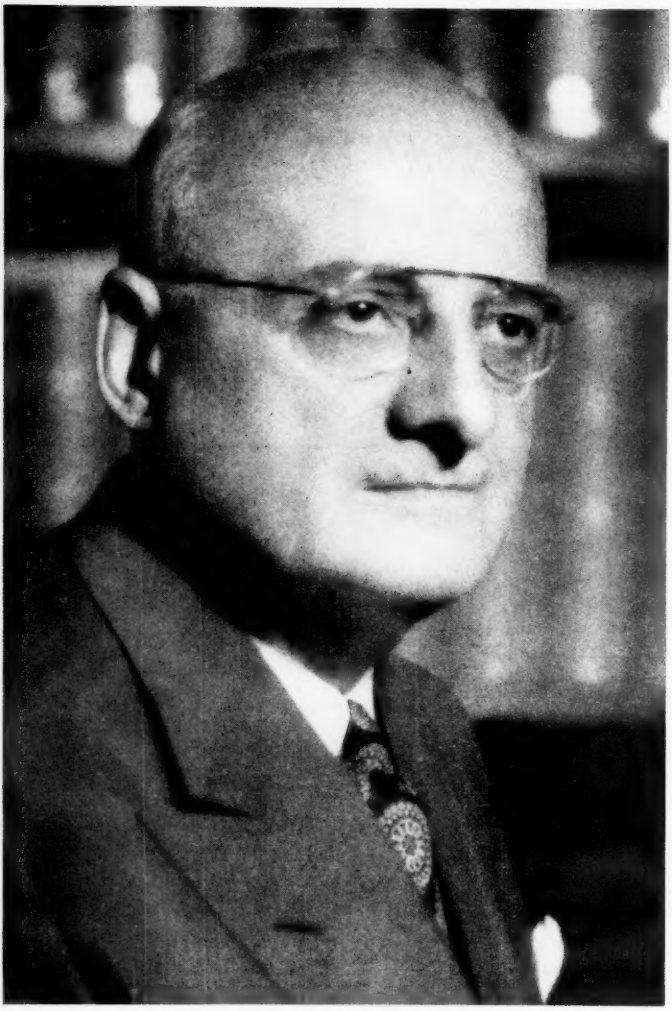
COMMITTEE AND BOARD MEETINGS

Sunday, April 4		
Board of Directors Meeting	8:00 a.m.	Card Room
Board of Regents Meeting	10:00 a.m.	Card Room
Tuesday, April 6		
Standardization (including sub-committees for Certification of Allergenic Extracts and Standardization of Aerosol Therapy)	9:00 a.m.	Card Room
Aerobiology	9:00 a.m.	Imperial Card Room
Public Education	10:00 a.m.	Imperial Card Room
Bylaws	10:00 a.m.	Card Room
Pediatric Allergy	11:00 a.m.	Card Room
Psychosomatic Allergy	11:00 a.m.	Imperial Card Room
Editorial Board	2:00 p.m.	Imperial Card Room
Pollen	2:00 p.m.	Card Room
New and Unused Therapeutics	3:00 p.m.	Imperial Card Room
Friday, April 9		
Dermatology	7:30 p.m.	Imperial Room
Saturday, April 10		
New Board of Regents	8:30 a.m.	Card Room



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MONDAY, APRIL 5, 1954

Morning Session—Surf Room

THE ALLERGIC NOSE

In the Chair: GILES A. KOELSCHE, M.D., Rochester, Minnesota

8:00—Registration—Lower Lounge Room

9:00—The Physiopathology of the Normal, Allergic, and Infected Nose
HERBERT H. HARRIS, M.D.,* Professor of Otolaryngology and Chairman of the Department, Baylor University College of Medicine, Houston, Texas

9:30—Hay Fever Producing Pollens
ROGER P. WODEHOUSE, Ph.D., Pearl River, New York

10:00—Household Allergens and Molds
HOMER E. PRINCE, M.D., Professor of Clinical Medicine, Baylor University College of Medicine, Houston, Texas

10:20—Uncommon Inhalant Allergens, Rusts and Smuts
FRED W. WITTICH, M.D., President, International Association of Allergology, Minneapolis, Minnesota

10:40—Common Food Allergens and Their Uncommon Adulterants
THERON G. RANDOLPH, M.D., Chicago, Illinois

11:00—Fundamentals of Testing Procedures
M. MURRAY PESHKIN, M.D., New York, New York, President, American College of Allergists

11:20—Symptomatic Treatment of the Allergic Nose
MARK H. MOTHERSILL, M.D., Outpatient Allergy Clinic, General Hospital, Indianapolis, Indiana

11:40—Injection Treatment of Allergic Disorders
J. WARRICK THOMAS, M.D., Assistant Professor, Clinical Medicine, Medical College of Virginia, Richmond, Virginia

BUFFET LUNCHEON—Imperial Room

12:30-2:00 P.M.

In the Chair: M. MURRAY PESHKIN, M.D., New York, New York
Guest Speaker: HANS SELYE, M.D.,*Montreal, Quebec, Canada

Stress and the Allergic Disorders

MONDAY, APRIL 5, 1954

Afternoon Session—Surf Room

THE ALLERGIC LUNG

In the Chair: LEON UNGER, M.D., Chicago, Illinois

2:00—Physiology of Respiration
LEON UNGER, M.D., Associate Professor, Northwestern Medical School; Attending Physician at Wesley Memorial and Cook County Hospitals, Chicago, Illinois

*By invitation

2:30—Physiopathology of Asthma, Emphysema and Bronchitis
MAURICE S. SEGAL, M.D., Clinical Professor of Medicine, Tufts College Medical School; Director, Department of Inhalational Therapy, Boston City Hospital, Boston, Massachusetts

3:00—Practical Procedures in the Diagnosis of Bronchial Asthma
SAMUEL J. PRIGAL, M.D., Assistant Professor of Medicine, New York Medical College, New York, New York

3:20—Chronic Progressive Pulmonary Failure
ROY A. OUER, M.D., Chief of Allergy Department, San Diego County and Mercy Hospitals, San Diego, California

3:40—Symptomatic Treatment of Bronchial Asthma in Adults
VINCENT J. DERBES, M.D., Associate Professor of Medicine and Director of Allergy Division, Department of Internal Medicine, Tulane University School of Medicine; Head of Allergy Department, Ochsner Clinic; Consultant in Allergy, U. S. Marine Hospital, New Orleans, Louisiana

4:00—Antimicrobial Agents in Acute and Chronic Lung Diseases
GEORGE E. ROCKWELL, M.D., Weslaco, Texas

4:30—Treatment of Asthma with ACTH and Cortisone
MAURICE S. SEGAL, M.D., Clinical Professor of Medicine, Tufts College Medical School; Director, Department of Inhalational Therapy, Boston City Hospital, Boston, Massachusetts

5:00—ABC's of Fluid and Electrolyte Metabolism—Their Importance in Allergic Diseases
FRED W. WITTICH, M.D., President, International Association of Allergology, Minneapolis, Minnesota

MONDAY, APRIL 5, 1954

Evening Panel—Surf Room—8:00-10:00 p.m.

THE STEROID HORMONES

Chairman: HANS SELYE, M.D.,* Montreal, Quebec, Canada
Endocrinology, Pharmacology, Dosage Schedule, Side Reactions and Results

Members: VINCENT J. DERBES, M.D., New Orleans, Louisiana
THERON G. RANDOLPH, M.D., Chicago, Illinois
MAURICE S. SEGAL, M.D., Boston, Massachusetts
GILES A. KOELSCHE, M.D., Rochester, Minnesota
ETHAN ALLAN BROWN, M.D., Boston, Massachusetts

MONDAY, APRIL 5, 1954

Evening Panel—Imperial Card Room—8:00-10:00 p.m.

PEDIATRIC PANEL: ALLERGY IN THE INFANT UNDER TWO

Chairman: BRET RATNER, M.D., New York, New York

Congenital Allergy
BRET RATNER, M.D., Professor of Clinical Pediatrics (Allergy) and Associate Professor of Immunology, New York Medical College; Attending Pediatrician, Flower and Fifth Avenue Hospitals; Director of Pediatrics, Sea View Hospital, New York, New York

Skin Tests in the Newborn and Early Infancy
EDWARD S. O'KEEFE, M.D., Member of the Board of Consultation of the Massachusetts General Hospital, Boston, Massachusetts; Consultant in Allergy, Lynn Hospital, Lynn, Massachusetts

*By invitation

Eczema and Urticaria
ALBERT V. STOESSER, M.D., Clinical Professor of Pediatrics and Director of the Pediatric Allergy Clinics, University of Minnesota Medical School, Minneapolis, Minnesota

Hay Fever
WALKER L. RUCKS, M.D., Chief, Department of Pediatrics, Baptist Memorial Hospital; Assistant Professor of Pediatrics, University of Tennessee, Memphis, Tennessee

Asthma
ETHEL M. DAVIS, M.D., Resident Instructor of Juvenile Research; Attending Pediatrician, Michael Reese Hospital; Director of Children's Allergy Clinic and Consultant in Allergy, Cook County Children's Hospital, Chicago, Illinois

Coelia Diseases and Gastrointestinal Allergy
C. COLLINS-WILLIAMS, M.D., Director of the Allergy Clinic, Hospital for Sick Children; Instructor in Pediatrics, University of Toronto Medical School, Toronto, Ontario, Canada

Prophylaxis of Allergy in Early Infancy
JEROME GLASER, M.D., Assistant Professor of Pediatrics, University of Rochester School of Medicine and Dentistry; Pediatrician-in-chief, Genesee Hospital, Rochester, New York

(Each speaker limited to 10 minutes, followed by questions and answers)

TUESDAY, APRIL 6, 1954

Morning Session—Surf Room

THE ALLERGIC SKIN

In the Chair: ADOLPH B. LOVEMAN, M.D., Louisville, Kentucky

9:00—Polymorphic Light Dermatoses
LEWIS CAPLAND, M.D.,* Miami Beach, Florida

9:20—Common Causes of Contact Dermatitis
GEOGRE L. WALDBOTT, M.D., Instructor, Wayne University College of Medicine, Detroit, Michigan

9:40—Symptomatic Treatment of Contact Dermatitis
ADOLPH B. LOVEMAN, M.D., Assistant Clinical Professor of Dermatology and Syphilology, University of Louisville School of Medicine, Louisville, Kentucky

10:00—Common Causes of Infantile Eczema
JEROME GLASER, M.D., Assistant Professor of Pediatrics, University of Rochester School of Medicine and Dentistry; Pediatrician-in-chief, Genesee Hospital, Rochester, New York

10:20—Symptomatic Treatment of Infantile Eczema
H. HARRIS PERLMAN, M.D., Associate Professor of Pediatrics, Graduate School of Medicine, University of Pennsylvania; Assistant Clinical Professor of Dermatology and Syphilology, New York Medical College; Pediatric Dermatologist, Pediatric Allergy Department, New York Medical College and Flower and Fifth Avenue Hospitals, New York, New York

10:40—Allergic Purpura
JEROME GLASER, M.D., Assistant Professor of Pediatrics, University of Rochester School of Medicine and Dentistry; Pediatrician-in-Chief, Genesee Hospital, Rochester, New York

11:00—Common Causes of Urticaria
LEWIS CAPLAND, M.D.,* Miami Beach, Florida

*By invitation

11:20—Dermatitis Medicamentosa

ADOLPH B. LOVEMAN, M.D., Assistant Clinical Professor of Dermatology and Syphilology, University of Louisville School of Medicine, Louisville, Kentucky

11:40—Light and Its Dermatological Effects

WILEY MITCHELL SAMS, M.D.,* Director, Department of Dermatology, James M. Jackson Memorial Hospital, Miami, Florida

BUFFET LUNCHEON—Imperial Room

12:30-2:00 P.M.

In the Chair: HOMER E. PRINCE, M.D., Houston, Texas

Guest Speaker: ALVAN L. BARACH, M.D.,* Clinical Professor of Medicine, Columbia University, New York, New York

Applied Physiologic Therapy in Bronchopulmonary Disease

TUESDAY, APRIL 6, 1954

Afternoon Session—Surf Room

MISCELLANEOUS ALLERGIC DISORDERS

In the Chair: HAL M. DAVISON, M.D., Atlanta, Georgia

2:00—Diagnosis and Treatment of Ocular Allergy

M. JAY FLIPSE, M.D.,* Miami, Florida

2:30—Diagnosis and Treatment of Allergy to Insects

BOEN SWINNY, M.D., Consultant in Allergy, Brooke General Hospital, United States Army, Ft. Sam Houston, Texas; Instructor in Allergy, Clinical Faculty, University of Texas; Instructor in Allergy, Clinical Faculty, Baylor University, San Antonio, Texas

3:00—Diagnosis and Treatment of Drug Allergy

LAWRENCE J. HALPIN, M.D., Cedar Rapids, Iowa

3:30—Diagnosis and Treatment of Physical Allergy

CECIL M. KOHN, M.D., Kansas City, Missouri

4:00—Bacteriological and Immunological Problems in the Diagnosis and Treatment of Bacterial Allergy

MORRIS SCHERAGO, D.V.M., Professor and Head of Department of Bacteriology, University of Kentucky, Lexington, Kentucky

4:30—Diagnosis and Treatment of Gastrointestinal Allergy

ORVAL R. WITHERS, M.D., Associate Professor of Medicine, University of Kansas School of Medicine, Lawrence and Kansas City, Kansas

5:00—Diagnosis and Treatment of Allergic Headache

HENRY D. OGDEN, M.D., Assistant Professor, Department of Medicine, Louisiana State University School of Medicine, New Orleans, Louisiana

*By invitation

TUESDAY, APRIL 6, 1954

Evening Panel—Surf Room—8:00-10:00 p.m.

ANTIHISTAMINIC AGENTS

Chairman: MARK H. MOTHERSILL, M.D., Indianapolis, Indiana
What they are, What they do, When are they useful, What side reactions may be expected, What are the results?
Members: S. H. JAROS, M.D., Scarsdale, New York
A. L. MAIETTA, M.D., Boston, Massachusetts
GEORGE E. ROCKWELL, M.D., Weslaco, Texas
S. WILLIAM SIMON, M.D., Dayton, Ohio

TUESDAY, APRIL 6, 1954

Evening Panel—Imperial Card Room—8:00-10:00 p.m.

MOLD ALLERGY

Chairman: HOMER E. PRINCE, M.D., Houston, Texas
Members: CLIFFORD H. KALB, M.D., Milwaukee, Wisconsin
ABRAM M. TARGOW, M.D., Los Angeles, California
MARIE B. MORROW, PH.D., Austin, Texas

WEDNESDAY, APRIL 7, 1954

Morning Session—Surf Room

THE ALLERGIC PATIENT

In the Chair: JOHN H. MITCHELL, M.D., Columbus, Ohio

9:00—Taking the History of the Allergic Patient
ETHAN ALLAN BROWN, M.D., Lecturer in Allergy, Tufts College Medical School; Physician-in-Chief, Allergy Section, Boston Dispensary Unit, New England Medical Center, Boston, Massachusetts

9:30—Heredity and the Allergic Patient
BRET RATNER, M.D., Professor of Clinical Pediatrics (Allergy) and Associate Professor of Immunology, New York Medical College; Attending Pediatrician, Flower and Fifth Avenue Hospitals; Director of Pediatrics, Sea View Hospital, New York, New York

10:00—Office Management of the Allergic Patient
JOHN D. GILLASPIE, M.D., Boulder, Colorado

10:30—Environmental Control of the Allergic Patient
L. O. DUTTON, M.D., El Paso, Texas

11:00—The Allergic Patient and His Diet
HARRY S. BERNTON, M.D., Clinical Professor of Medicine, Howard University; Clinical Specialist in Allergy, Allergens Research Division, U. S. Department of Agriculture; Allergist to Providence Hospital; Allergist to Doctor's Hospital, Washington, D. C.

11:30—Emotional Problems of the Allergic Patient
JOHN H. MITCHELL, M.D., Assistant Clinical Professor of Medicine, Ohio State University College of Medicine, Columbus, Ohio

12:00—The Role of Infection in the Allergic Patient
SAMUEL J. PRIGAL, M.D., Assistant Professor of Medicine, New York Medical College, New York, New York

BUFFET LUNCHEON—Imperial Room

12:30-2:00

In the Chair: LAWRENCE J. HALPIN, M.D., Cedar Rapids, Iowa

Guest Speaker: HOMER F. MARSH, Ph.D.,* Associate Dean, University of Miami School of Medicine, Miami, Florida

Some Immunologic Aspects of Allergy

WEDNESDAY, APRIL 7, 1954

Afternoon Session—Surf Room

THE ALLERGIC STATE

In the Chair: J. WARRICK THOMAS, M.D., Richmond, Virginia

2:00—Allergic Skin Reactions and the Theory of Histamine
HAROLD A. ABRAMSON, M.D., Associate Physician and Chief, Allergy Clinic, The Mount Sinai Hospital, New York, New York

2:30—Endocrines and Allergy
S. H. JAROS, M.D., Chief, Allergy Clinic, Division of Internal Medicine, Grasslands Hospital, Valhalla, New York

3:00—The Pharmacology of Allergic Disorders
MORRIS A. KAPLAN, M.D., Assistant Professor of Medicine, Chicago Medical School; Attending Assistant, Michael Reese Hospital; Attending Allergist, Mandel Clinics, Michael Reese Hospital, Chicago, Illinois

3:30—Non-Specific Measures, and When to Use Them
BOEN SWINNY, M.D., Consultant in Allergy, Brooke General Hospital, United States Army, Ft. Sam Houston, Texas; Instructor in Allergy, Clinical Faculty, University of Texas; Instructor in Allergy, Clinical Faculty, Baylor University, San Antonio, Texas

4:00—Individualization of Treatment
WALKER L. RUCKS, M.D., Chief, Department of Pediatrics, Baptist Memorial Hospital; Assistant Professor of Pediatrics, University of Tennessee, Memphis, Tennessee

4:30—Future Research in Allergy
R. L. MAYER, M.D., Summit, New Jersey

WEDNESDAY, APRIL 7, 1954

Evening Session—Surf Room—8:00-10:00 p.m.

ANY QUESTIONS?

Chairman: J. WARRICK THOMAS, M.D., Richmond, Virginia
Members: GILES A. KOELSCHE, M.D., Rochester, Minnesota
MORRIS A. KAPLAN, M.D., Chicago, Illinois
LAWRENCE J. HALPIN, M.D., Cedar Rapids, Iowa
GEORGE E. ROCKWELL, M.D., Weslaco, Texas
BRET RATNER, M.D., New York, New York
A. L. MAIETTA, M.D., Boston, Massachusetts
ETHAN ALLAN BROWN, M.D., Boston, Massachusetts

*By invitation

WEDNESDAY, APRIL 7, 1954

Evening Psychosomatic Workshops—8:00-10:00 p.m.

EMOTIONAL FACTORS IN ALLERGIC DISORDERS

Chairman: BOEN SWINNY, M.D., San Antonio, Texas

Roney Plaza Hotel—Imperial Card Room

1. **Psychoanalytically Oriented Interviews**—Tape Recording
   Moderator: HAROLD A. ABRAMSON, M.D., Associate Physician and Chief, Allergy Clinic, The Mount Sinai Hospital, New York, New York
   Reporter: M. MURRAY PESHKIN, M.D., Consulting Allergist, Mount Sinai Hospital, New York, New York

Wofford Beach Hotel—Coral Room

2. **An Actual Diagnostic Play Session with an Allergic Child**
   Moderator: DOROTHY W. BARUCH, Ph.D.,* Beverley Hills, California
   Reporter: HAL M. DAVISON, M.D., Chief of Medicine and Instructor in Allergy, Georgia Baptist Hospital, Atlanta, Georgia

Promenade Hotel—Card Room

3. **A Psychotherapeutic Group Interview with the Parents of Allergic Children**
   Moderator: HYMAN MILLER, M.D., Beverly Hills, California, Associate Clinical Professor of Medicine, University of California at Los Angeles Medical School, Los Angeles, California
   Reporter: BENNETT KRAFT, M.D., Lecturer in Allergy, Indianapolis General Hospital, Indianapolis, Indiana

Surfside Plaza Hotel—Card Room

4. **Tape Recordings of Interviews with Allergic Patients**
   Moderator: JOHN H. MITCHELL, M.D., Associate Professor, Department of Medicine, Ohio State University, Columbus, Ohio
   Reporter: HOMER E. PRINCE, M.D., Professor of Clinical Medicine, Baylor University College of Medicine, Houston, Texas

Each group is limited to 40 registrants, and it may be necessary to assign some to groups other than their choice.

Attendance for the Friday evening summaries of the Workshops is unlimited.

*By invitation

MONDAY THROUGH FRIDAY—APRIL 5-9

(Room to be announced)
9:00 a.m.-5:00 p.m.

OFFICE AND LABORATORY PROCEDURES

STEPHEN D. LOCKEY, M.D., Lancaster, Pennsylvania, and Associates

1. **Management of the allergic patient; history taking; examples of history and testing forms in common use.**
2. **Lectures and demonstrations on the extracting and preparation of house dust, polyvalent epidermal, pollen, mold and food extracts.**
3. **Preparation and dilution of testing materials.**
4. **Demonstrations of various methods of testing: dermal, endermal, patch, intra-ocular, insufflation, et cetera.**
5. **Preparation of polyvalent epidermal, pollen and mold treatment sets.**
6. **Preparation of autogenous vaccines.**
7. **Miscellaneous laboratory procedures; demonstrations of various simple laboratory procedures, pulmonary function tests, et cetera.**

Fee for the Instructional Course is $65 which includes three round table buffet luncheons.

This Course has been approved for formal credit by the Commission on Education of the American Academy of General Practice.

TECHNICAL EXHIBITS

During the mid-morning and mid-afternoon of each of the three days of the Scientific Program, it is imperative that a half hour be allotted for visiting the exhibits. The chairman of each section is instructed to call a recess at this time, and participants have received printed instructions from the Over-all Chairman to prepare their papers so as to adhere to the time limits.

We are obligated by contract to extend this courtesy to our exhibitors. If it were not for them, it would be impossible to finance annually a successful program on an extensive scale. You will find this year's Technical Exhibits extraordinary, and worthy of your time. The representatives will be pleased to receive any suggestions or comments you may make. Many of these exhibitors are advertisers in the ANNALS OF ALLERGY, and/or Sustaining Members of the College.

Your co-operation in showing our appreciation to the Technical Exhibitors is earnestly requested.

Decennial Congress

(Preliminary Program—subject to minor changes)

WEDNESDAY, APRIL 7, 1954

2:00-5:30 P.M.

Registration—Lower Lounge Room
Scientific Program of The American Association for Mycological Investigation. (See complete program, page 66.)

8:00-10:00 P.M.

Emotional Factors in Allergic Disorders
Four Psychosomatic Workshops. (See details, page 57.)

THURSDAY, APRIL 8, 1954

Morning Session—Surf Room

GENERAL SESSION

In the Chair: GILES A. KOELSCHE, M.D., Rochester, Minnesota

9:00—Clinical Experiences with "Pyronil" and "Co-Pyronil"
MARK H. MOTHERSILL, M.D., Outpatient Allergy Clinic, General Hospital, Indianapolis, Indiana

9:15—Sustained-Release Antihistaminic Medication
MAYER A. GREEN, M.D., Director of the Department of Allergy, Columbia Hospital, Pittsburgh, Pennsylvania

9:30—Clinical Evaluation of a New Antihistamine Drug, F. C. 1
MORRIS A. KAPLAN, M.D., Assistant Professor of Medicine, Chicago Medical School; Attending Assistant, Michael Reese Hospital; Attending Allergist, Mandel Clinics, Michael Rees Hospital, Chicago, Illinois
A. L. AARONSON, M.D., Chicago, Illinois
N. J. EHRLICH, M.D., Chicago, Illinois
Discussion: RALPH BOWEN, M.D., Associate Professor of Medicine, Baylor College of Medicine; Special Lecturer Pediatrics, Texas Medical Branch, Galveston, Texas
LAWRENCE J. HALPIN, M.D., Cedar Rapids, Iowa

9:55—Tissue Changes in Allergy Before and After ACTH Therapy
BEN Z. RAPPAPORT, M.D.,* Clinic Associate Professor of Medicine and Head Allergy Unit, University of Illinois College of Medicine, Chicago, Illinois
Discussion: HARRY S. BERNTON, M.D., Clinical Professor of Medicine, Howard University; Clinical Specialist in Allergy, Allergens Research Division, U. S. Department of Agriculture; Allergist to Providence Hospital; Allergist to Freedman Hospital, Washington, D. C.

10:30—RECESS TO VISIT EXHIBITS

11:00—The Hypnotic Investigation of the Asthmatic Patient
HAROLD ROSEN, M.D.,* Baltimore, Maryland
Discussion: HERMAN SELINSKY, M.D.,* Miami, Florida

11:20—Hypersensitiveness to Human Pituitary
RALPH HALE, M.D., Allergy Clinic, University of Kansas Medical Center, Kansas City, Kansas
Discussion: FRANK A. SIMON, M.D., Associate Clinical Professor of Medicine, University of Louisville, Louisville, Kentucky

*By invitation

11:40—Vascular Headaches

ROY A. OUER, M.D., Chief of Allergy Department, San Diego County and Mercy Hospitals, San Diego, California

Discussion: HOMER E. PRINCE, M.D., Professor of Clinical Medicine, Baylor University College of Medicine, Houston, Texas

12:00—Chronic Ulcerative Colitis and Regional Enteritis Due to Allergy

ALBERT H. ROWE, M.D., Allergist, Samuel Merritt Hospital, Oakland Naval Hospital, Oakland, California; Allergist, Cowell Hospital, Berkeley, California; Lecturer in Medicine, University of California Medical School, San Francisco, California

and

ALBERT ROWE, JR., M.D., Oakland, California

Discussion: VINCENT J. DERBES, M.D., Associate Professor of Medicine and Director of Allergy Division, Department of Internal Medicine, Tulane University School of Medicine; Head of Allergy Department, Ochsner Clinic; Consultant in Allergy, U. S. Marine Hospital, New Orleans, Louisiana

and

ORVAL R. WITHERS, M.D., Associate Professor of Medicine, University of Kansas School of Medicine, Lawrence and Kansas City, Kansas

12:30—ROUND TABLE LUNCHEON—Imperial Room

Moderator: J. WARRICK THOMAS, M.D., Richmond, Virginia

Pitfalls in the Diagnosis and Management of Asthma

Panel Members:

MAYER A. GREEN, M.D., Pittsburgh, Pennsylvania
LEON UNGER, M.D., Chicago, Illinois
VINCENT J. DERBES, M.D., New Orleans, Louisiana
ALBERT V. STOESSER, M.D., Minneapolis, Minnesota
DAVID R. THOMAS, JR., M.D., Augusta, Georgia

THURSDAY, APRIL 8, 1954

Afternoon Session—Surf Room

GENERAL SESSION

In the Chair: MAYER A. GREEN, M.D., Pittsburgh, Pennsylvania

2:00—A Classification of Bronchial Asthma

ETHAN ALLAN BROWN, M.D., Lecturer in Allergy, Tufts College Medical School; Physician-in-Chief, Allergy Section, Boston Dispensary Unit, New England Medical Center, Boston, Massachusetts

and

LAWRENCE J. HALPIN, M.D., Cedar Rapids, Iowa

2:20—Cathode Ray Therapy for Generalized Eczematous Eruptions

JOHN L. FROMER, M.D., Chief, Allergy and Dermatology, Lahey Clinic, Boston, Massachusetts

Discussion: ADOLPH B. LOVEMAN, M.D., Assistant Clinical Professor of Dermatology and Syphilology, University of Louisville School of Medicine, Louisville, Kentucky

2:40—Clinical Observations on the Use of Histamine in Medical Practice

CLARENCE BERNSTEIN, M.D., Orlando, Florida

Discussion: HOMER E. PRINCE, M.D., Professor of Clinical Medicine, Baylor University College of Medicine, Houston, Texas

3:00—RECESS TO VISIT EXHIBITS

3:30—Standardization and Antigenic Analysis of Pollen Extracts by Gel Diffusion

ROGER P. WODEHOUSE, Ph.D., Pearl River, New York

Discussion: ETHAN ALLAN BROWN, M.D., Lecturer in Allergy, Tufts College Medical School; Physician-in-Chief, Allergy Section, Boston Dispensary Unit, New England Medical Center, Boston, Massachusetts

3:50—The Basic Mechanisms of Anaphylaxis and Allergy

BRET RATNER, M.D., Professor of Clinical Pediatrics (Allergy) and Associate Professor of Immunology, New York Medical College; Attending Pediatrician, Flower and Fifth Avenue Hospitals; Director of Pediatrics, Sea View Hospital, New York, New York

Discussion: HAROLD A. ABRAMSON, M.D., Associate Physician and Chief, Allergy Clinic, The Mount Sinai Hospital, New York, New York

4:25—Selection of Molds for Therapy

HOMER E. PRINCE, M.D., Professor of Clinical Medicine, Baylor University College of Medicine, Houston, Texas

Discussion: LAWRENCE J. HALPIN, M.D., Cedar Rapids, Iowa

4:45—Rheumatic Fever or Allergic Carditis?

S. H. JAROS, M.D., Chief, Allergy Clinic, Division of Internal Medicine, Grasslands Hospital, Valhalla, New York

Discussion: HARRY MARKOW, M.D., Attending Allergist, Beth El Hospital; Chief Clinician, Beth El Allergy Clinic, Brooklyn, New York

5:05—Specific Versus Anaspecific Therapy in Two Hundred Asthmatic Patients

GONZALO ESTRADA DE LA RIVA, M.D., Consulting Allergist of the French Hospital, New York, New York; Chief of the Allergy Department, Clinic of the Asociación Canaria; Associate Professor in Experimental Pathology, University of Havana, Havana, Cuba

Discussion: FRANCISCO DE LA TORRE MADRAZO, M.D., Chief of Allergy Department, Hospital General de la Policia Nacional; Chief of Allergy Department, The Institucion Nacional de Examen y Diagnostico, Havana, Cuba

6:00—COCKTAIL HOUR—GARDEN PATIO

Courtesy of the Schering Corporation, Bloomfield, New Jersey

7:00—FLORIDA FIESTA NIGHT—PALM PATIO

Banquet—Aquatic Show—Dancing

FRIDAY, APRIL 9, 1954

Morning Session—Surf Room

SECTION ON PEDIATRIC ALLERGY

In the Chair: JEROME GLASER, M.D., Rochester, New York

9:00—Climate as an Influencing Factor in Childhood Allergy: A Clinical Evaluation
MEYER B. MARKS, M.D.,* Attending Pediatrician, Mount Sinai and St. Francis Hospitals; Visiting Pediatrician, Jackson Memorial Hospital, Miami, Florida
Discussion opened by FRANK C. METZGER, M.D., Tampa, Florida

9:20—Fever of Allergic Origin
JULIA BAKER, M.D., Medical Board of the British American Cowdry Hospital; Chairman of the Polio Relief Committee, Mexico City, D.F., Mexico
Discussion opened by HAL M. DAVISON, M.D., Atlanta, Georgia

9:40—Acute and Chronic Urticaria and Angioedema in Children and Young Adults
SHELDON C. SIEGEL, M.D., and JOSEPH G. BERGERON, M.D.*
Presented by Dr. Siegel, Capt., M.C., A.U.S.; Clinical Assistant Professor of Pediatrics, University of Texas; Lackland Air Force Base Hospital, San Antonio, Texas
Discussion opened by JOSEPH G. BERGERON, M.D.

10:00—Electrical Pneumatographs in a Pediatric Allergy Clinic
HOWARD G. RAPAPORT, M.D., Bernard Sklarofsky, B.A.* and HENRIETTE H. GETTNER, M.A.*
Presented by Dr. Rapaport, Pediatrician in Charge of the Pediatric Allergy Clinic, Mt. Sinai Hospital, New York, New York
Discussion opened by HAROLD A. ABRAMSON, M.D., New York, New York

10:20—Incidence and Treatment of Headaches Due to Allergy in Children
ALBERT V. STOESSER, M.D., and LLOYD S. NELSON, M.D.*
Presented by Dr. Stoesser, Clinical Professor of Pediatrics and Director of the Pediatric Allergy Clinics, University of Minnesota Medical School, Minneapolis, Minnesota
Discussion opened by HENRY D. OGDEN, M.D., New Orleans, Louisiana

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There will be a short discussion following each paper

10:30—RECESS TO VISIT EXHIBITS

11:00—The Relationship Between a Careful Dietary Study and Cortisone Therapy in the Treatment of Infantile Eczema
EDWARD S. O'KEEFE, M.D., Member of the Board of Consultation of the Massachusetts General Hospital, Boston, Massachusetts; Consultant in Allergy, Lynn Hospital, Lynn, Massachusetts
Discussion opened by THERON G. RANDOLPH, M.D., Chicago, Illinois

11:20—The Allergic Aspects of Celiac Disease
C. COLLINS-WILLIAMS, M.D., and J. HARRY EBBS, M.D.*
Presented by Dr. Collins-Williams, Director of the Allergy Clinic, Hospital for Sick Children; Instructor in Pediatrics, University of Toronto Medical School, Toronto, Ontario, Canada
Discussion opened by WARREN W. QUILLIAN, M.D.,* Coral Gables, Florida

*By invitation.

11:40—The Colicky Baby

FREDERICK J. MARTIN, M.D.,* Instructor in Pediatrics, University of Rochester School of Medicine and Dentistry; Attending Pediatrician, St. Mary's Hospital, Rochester, New York

Discussion opened by W. AMBROSE MCGEE, M.D.,* Palm Beach, Florida

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There will be a short discussion following each paper

12:30—ROUND TABLE LUNCHEON—Pediatric Allergy—Imperial Room

GASTROINTESTINAL ALLERGY IN CHILDREN

Moderator: C. COLLINS-WILLIAMS, Toronto, Ontario, Canada

Elimination Diets

ALBERT H. ROWE, M.D., Allergist, Samuel Merritt Hospital, Oakland Naval Hospital, Oakland, California; Allergist, Cowell Hospital, Berkeley, California; Lecturer in Medicine, University of California Medical School, San Francisco, California

Denatured Diets

BRET RATNER, M.D., Professor of Clinical Pediatrics (Allergy) and Associate Professor of Immunology, New York Medical College; Attending Pediatrician, Flower and Fifth Avenue Hospitals; Director of Pediatrics, Sea View Hospital, New York, New York

Allergic Coeliac Syndrome and Allergic Diarrhea

DOUGLAS E. JOHNSTONE, M.D.,* Assistant Pediatrician, Strong Memorial Hospital and Gennessee Hospital; Attending Pediatrician, Pediatric Allergy Clinic, Strong Memorial Hospital; Instructor in Pediatrics, University of Rochester School of Medicine, Rochester, New York

Ulcerative Colitis and Regional Enteritis

ALBERT H. ROWE, M.D., Oakland, California

Closing Remarks

C. COLLINS-WILLIAMS, M.D., Director of the Allergy Clinic, Hospital for Sick Children; Instructor in Pediatrics, University of Toronto Medical School, Toronto, Ontario, Canada

12:30—ROUND TABLE LUNCHEON—Otorhinolaryngologic Allergy—Imperial Card Room

Moderator: LAWRENCE K. GUNDRUM, M.D., Los Angeles, California

Cytology of the Secretions of the Ear, Nose and Throat

LAWRENCE K. GUNDRUM, M.D., Los Angeles, California

Allergy of the Ear

HUGH A. KUHN, M.D., Section Otolaryngology, A.M.A., Former President, American Society of Ophthalmologic and Otolaryngologic Allergy, Hammond, Indiana

Allergy in its Relation to the Tonsils and Adenoid

KENNETH L. CRAFT, M.D., Department of Otolaryngology, Indiana University School of Medicine, Indianapolis, Indiana

A Clinical Dietary History Form for Otolaryngology

RAY M. MOOSE, M.D., San Bernardino, California

General Discussion

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*By invitation

FRIDAY, APRIL 9, 1954

Afternoon Session—Surf Room

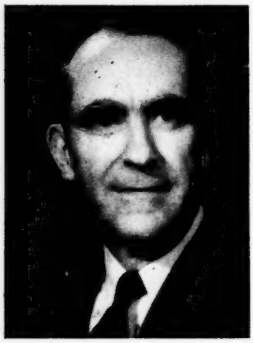
In the Chair: JOHN D. GILLASPIE, M.D., Boulder, Colorado

2:00—Presidential Address

M. MURRAY PESHKIN, M.D., Consulting Allergist, Mount Sinai Hospital, New York, New York

2:20—Introduction of Homer E. Prince, M.D., President-Elect

2:30—Individuality as a Factor in Resistance to Disease



Guest Speaker

JOHN W. GOWEN, Ph.D., Professor of Genetics, Iowa State College of Agriculture and Mechanic Art, Ames, Iowa

3:00—RECESS TO VISIT EXHIBITS

3:30—Business Meeting

FRIDAY, APRIL 9, 1954

Evening Session—Surf Room

DERMATOLOGIC ALLERGY

In the Chair: ADOLPH B. LOVEMAN, M.D., Louisville, Kentucky

7:30—Discussion of Committee Matters

.... DERMATOLOGIC COMMITTEE members

8:00—Polymorphic Light Dermatoses

LEWIS CAPLAND, M.D.,* Miami Beach, Florida

8:30—Histopathology of Allergic Dermatoses

HERMANN PINKUS, M.D.,* Attending Physician, Department of Dermatology, Detroit Receiving Hospital; Associate Professor of Dermatology, Wayne University College of Medicine, Detroit, Michigan

9:00—A New Approach to the Treatment of Chronic Urticaria

ARMAND E. COHEN, M.D.,* Clinical Assistant Professor of Medicine and Director Allergy Clinic, Louisville Medical School, Louisville, Kentucky

*By invitation

9:30—Round Table Discussion

ALEX S. FRIEDLAENDER, M.D., Instructor in Clinical Medicine, Wayne University College of Medicine, Detroit, Michigan
ALBERT H. ROWE, M.D., Allergist, Samuel Merritt Hospital, Oakland, Naval Hospital, Oakland, California; Allergist, Cowell Hospital, Berkeley, California; Lecturer in Medicine, University of California Medical School, San Francisco, California
HERMANN PINKUS, M.D.,* Monroe, Michigan
LEWIS CAPLAND, M.D.,* Miami Beach, Florida
ARMAND E. COHEN, M.D.,* Louisville, Kentucky
ADOLPH B. LOVEMAN, M.D., Assistant Clinical Professor of Dermatology and Syphilology, University of Louisville School of Medicine, Louisville, Kentucky

FRIDAY, APRIL 9, 1954

Evening Session—Ocean Lounge

7:30-10:00 P.M.

CLINICAL PANEL ON PSYCHOSOMATIC ALLERGY

Moderator: HYMAN MILLER, M.D., Beverly Hills, California

The moderators and reporters from each workshop of Wednesday evening on EMOTIONAL FACTORS IN ALLERGIC DISORDERS, will summarize their findings.

Procedure:

1. Brief summaries on what was seen and heard at the workshops, as well as the conclusions of the group in regard to the application of this information to private practice.
2. Questions to members of the panel, and comments and discussion from the floor.

SATURDAY, APRIL 10, 1954

Morning Session—Surf Room

SECTION ON OPHTHALMIC OTORHINOLARYNGOLOGIC ALLERGY

In the Chair: HUGH A. KUHN, M.D., Hammond, Indiana

9:00—Allergic Dermatitis in Ophthalmology and Otolaryngology

KENNETH L. CRAFT, M.D., Department of Otolaryngology, Indiana Univerity School of Medicine, Indianapolis, Indiana

Discussants: GEORGE L. WALDBOTT, M.D., Detroit, Michigan
and
L. DELL HENRY, M.D., Lecturer in Speech Pathology, Department of Speech; Staff Physician, Speech Clinic, University of Michigan, Ann Arbor, Michigan

9:30—All is Not Asthma that Wheezes—Broncholith

FREDERICK D. DROEGE, M.D., Sarasota, Florida

Discussant: BENNETT KRAFT, M.D., Lecturer in Allergy, Indianapolis General Hospital, Indianapolis, Indiana

10:00—Relation of Allergy to Ménière's Syndrome Complex

LAWRENCE K. GUNDRUM, M.D., Los Angeles, California

Discussant: A. J. KUHN, M.D.,* Mayo Clinic, Rochester, Minnesota

*By invitation

10:30—RECESS TO VISIT EXHIBITS

11:00—Observations on Allergic Sinusitis in Children
JOSEPH W. HAMPSEY, M.D., Pittsburgh, Pennsylvania
Discussant: B. M. BARRETT, M.D.,* Tulane University of Louisiana School of Medicine, New Orleans, Louisiana

11:30—Local use of a Suspension of Cortogen Acetate with Chlor-Trimeton Maleate in the Treatment of Allergic Rhinitis of Pollen Origin
WILLIAM H. EVANS, M.D., Youngstown, Ohio

12:00—The Otologic Manifestation of Allergy
CLYDE F. ELKINS, M.D., Lubbock, Texas

*By invitation

Association of Allergists for Mycological Investigation, Inc.

Card Room

WEDNESDAY, APRIL 7, 1954

Scientific Program under the direction of The Association of Allergists for Mycological Investigations, Inc., to which all interested allergists are invited.

2:00—Preliminary Report on Air-borne Bacterial Populations, and Preliminary Report on Clinical Experiences with Air-borne Bacterial Antigens
L. O. DUTTON, M.D., Chairman, Subcommittee on Air-borne Bacterial Studies

2:40—Air-borne Populations—Additional survey studies of previously unreported areas and resurvey studies
MARIE B. MORROW, Ph.D., Mycologist

3:40—Preliminary Report of Testing and Treatment with Pathogenic Fungi, Trichophyton and Monilia Albicans, Prepared by Technique 33
BOEN SWINNY, M.D., Chairman, Subcommittee on the Study of Extracts of Pathogenic Fungi

Decennial Congress

TO BE READ BY TITLE

Evaluation of Maternal Rejection Theory in Allergy
HAROLD A. ABRAMSON, M.D., New York, New York

Systemic Reactions Following Scratch Testing in Allergy
RALPH BOWEN, M.D., Houston, Texas

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SIDNEY FRIEDLAENDER, M.D., Detroit, Michigan

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GEORGE P. HECKEL, M.D.,* Rochester, New York

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A. L. MAIETTA, M.D., Boston, Massachusetts

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HENRY D. OGDEN, M.D., New Orleans, Louisiana

Atmospheric Pollens and Mold Spores in the Asheville Area
DAVID M. PIPES, M.D., Asheville, North Carolina

Blood Chemistry and Nutritional Assay Studies in the Allergic State
NATHAN E. SILBERT, M.D., Lynn, Massachusetts

The Use of Chlor-Trimeton in the Prevention of Blood Transfusion Reactions
S. WILLIAM SIMON, M.D., Dayton, Ohio
WILLIAM G. ECKMAN, JR., M.D.,* Dayton, Ohio

Antigenic Analysis by Gel Diffusion, I. Ragweed Pollen
ROGER P. WODEHOUSE, Ph.D., Pearl River, New York

*By invitation.

Entertainment

THURSDAY, APRIL 8, 1954

12:30—Ladies Luncheon and Style Show—Patio

6:00—Cocktail Party—Patio

(Courtesy The Schering Corporation)

7:00—Florida Fiesta Night—Patio and Olympic Pool

Banquet—Aquatic Show—Dancing
(Wine—Courtesy The Nepera Chemical Company)

FRIDAY, APRIL 9, 1954

10:30 to 5:00—Inland waterway cruise of Miami Beach—Luncheon at Vizcaya (Deering Estate)

The boat leaves from the Roney Plaza Yacht Basin on Collins Avenue at 10:30 a.m.

SATURDAY, APRIL 10, 1954

1:30—Horse Racing—Gulf Stream Park

The American College of Allergists Handicap. Transportation is readily available.

We are indeed grateful to the sponsors who have furnished the necessary funds for entertainment and scholarships for the Decennial Congress. A list of these sponsors will appear in the final program.

TO ALL DECENNIAL CONGRESS REGISTRANTS
WELCOME TO MIAMI BEACH!

You fortunately chose one of the very best times of the year to visit our city and practically anything you want to do except skiing, sleigh riding, and tobogganning is available to you. Our committee has arranged the following activities for your enjoyment and you will be glad you came to this convention, if you partake of these activities:

1. **Thursday, April 8, 12:30—Ladies' Luncheon and Fashion Show in the Patio at the Roney Plaza Hotel.** This activity is arranged so that you will have plenty of time to rest before the banquet that night.
2. **Thursday, April 8, 6:00—Cocktail Party—Patio,** followed by **Florida Fiesta Night**—Banquet—Aquatic Show—Dancing.
3. **Friday, April 9—Boat tour of the islands of Miami Beach and beautiful Vizcaya (Deering Estate).**—The boat leaves from the Roney Plaza Yacht Basin on Collins Avenue. The trip starts at 10:30 A.M. and you will be returned to the hotel at 5:00 P.M. Luncheon will be served at the beautiful Vizcaya, at noon.
4. **Saturday, April 10, 1:30 P.M.—Horseracing at Gulf Stream Park.** The feature race that afternoon will be known as The American College of Allergists Handicap. Transportation is readily available.

In addition to the above-planned activities, a Hostess Table will be staffed throughout the convention, and every effort will be made to help you arrange for any other activity you may desire. The following are some of the activities available to you and your family. Most of them are well worth staying a few extra days in Miami Beach to enjoy:

1. You can just relax and enjoy the sunshine at your hotel if you need a rest.
2. Night time activities include dog racing, Jai Alai, and night clubs.
3. There are other night time activities, such as dancing at all the hotels, concerts at the City Auditorium by the University of Miami orchestra, and legitimate theater presentations.
4. Those who are athletically inclined can indulge in golf at any one of the three courses on Miami Beach, tennis, swimming, water skiing.
5. If sightseeing is your major interest, we can arrange for trips to the Fairchild Gardens, Parrot Jungles, Alligator Farms, Fruit Groves, and Orchid Farms. Also remember that you are a very short distance from Nassau and Havana. Air flight to these two places is just sixty minutes.
6. Fishing of all types is available in Miami Beach, and arrangements can be made for charter or party boats.

Hostess Committee:

MRS. NELSON ZIVITZ, *Chairman*
MRS. HAROLD RAND
MRS. JAMES H. PUTMAN
MRS. HOMER E. PRINCE—*Honorary Hostess*

Technical Exhibits

Almay Beauty Preparations, Division of Schieffelin & Co.	New York, New York
The Armour Laboratories	Chicago, Illinois
Ernst Bischoff Company, Inc.	Ivoryton, Connecticut
The Borden Company	New York, New York
Bruce Publishing Company	Saint Paul, Minnesota
Burroughs Wellcome & Co. (U.S.A.), Inc.	Tuckahoe, New York
Center Laboratories, Inc.	Port Washington, New York
Ciba Pharmaceutical Products, Inc.	Summit, New Jersey
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AEROSOLS OF PANCREATIC DORNASE IN BRONCHOPULMONARY DISEASE

A. SALOMON, M.D., J. A. HERCHFUS, M.D., and M. S. SEGAL, M.D., F.A.C.A.
Boston, Massachusetts

MANY reports have appeared within the past few years on the use of enzymes of various origins for enzymatic debridement of fibrinopurulent exudates in a variety of conditions: plueral, abdominal and other empyemas, hemothorax, chronic ulcers, osteomyelitis, infected surface wounds, burns, et cetera.[1,2,5,9,10,12] More recently, much attention has been given to the problem of liquefaction and removal of viscid and mucopurulent secretions from the tracheobronchial passages with the help of enzymes.[18,19] The harmful potentialities of these secretions, by obstructing airways and acting as a culture medium for infectious microorganisms, is recognizable. The rapid and safe evacuation of these secretions in the simplest possible manner is a problem of great importance.

*Pancreatic Dornase.**—Desoxyribonucleoprotein is an important constituent of purulent exudate and it determines the character, viscosity and amount of sediment of such exudates.[15] Desoxyribonuclease, whether of streptococcal origin (streptodornase) or of pancreatic origin (Pancreatic Dornase), is a pus-liquefying enzyme and is capable of degrading desoxyribonucleoprotein.[16,17] Streptokinase is the fibrinolytic principle obtained from streptococcal concentrates.

The action of Pancreatic Dornase is primarily one of depolymerization, and but little degradation of desoxyribonucleoprotein occurs.[6] The absence of appreciable amounts of noxious degradation products, which might be absorbed into the system of the patient, permits the use of Pancreatic Dornase with little systemic effect.

Pharmacology.—Pancreatic desoxyribonuclease (Pancreatic Dornase) is prepared from beef pancreas. Its activity is measured by the rate of reduction of the viscosity of thymonucleic acid, prepared from thymus glands and freed of protein.

Lyophilized Pancreatic Dornase, dissolved in saline (0.7 per cent) with magnesium sulfate (0.2 per cent) and kept at room temperature, has been

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*The Pancreatic Dornase for these studies kindly supplied by Sharp & Dohme, Inc., West Point, Pennsylvania.

found to retain its activity for six to eight hours and to lose one-third of its activity at the end of twenty-four hours.[14]

The influence of antibiotics on Pancreatic Dornase was studied *in vitro*. The drugs tested were Potassium Penicillin G, Dihydrostreptomycin, Baci-

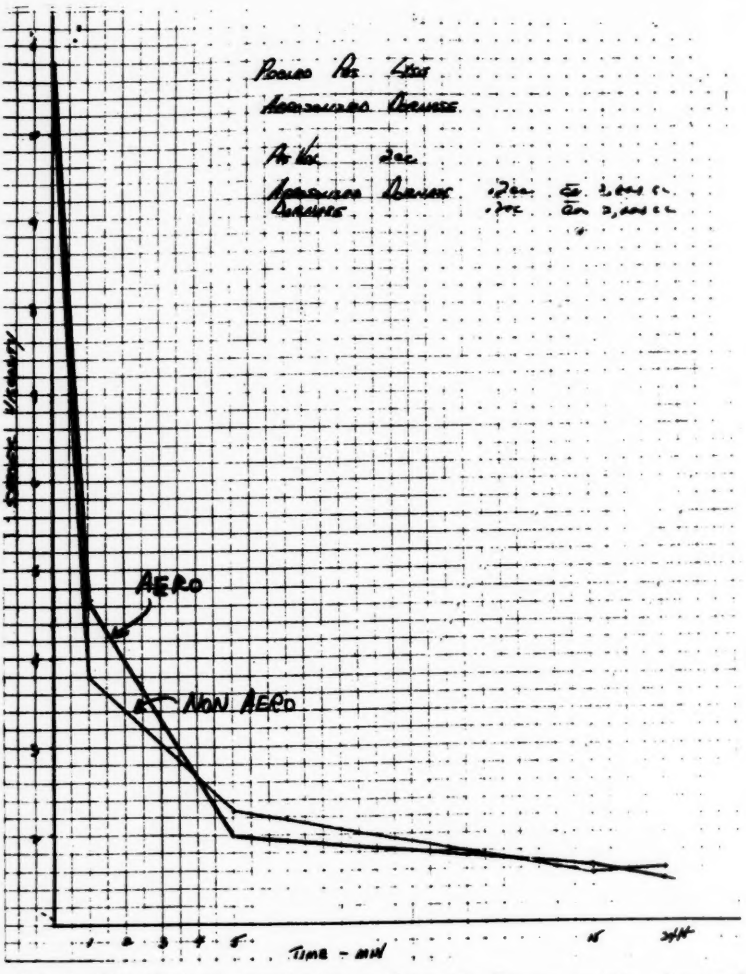

Fig. 1. The effect of aerosolization on Pancreatic Dornase activity. Reprinted through the courtesy of Howard G. Reiser, M.D.[8]

tracin, Polymixin B. sulfate, Aureomycin, Terramycin, Chloromycetin and Tyrothricin. The results of these studies indicated that the various antibiotics have no significant effect on Pancreatic Dornase.[14]

Enzymatic Lysis of Pus.—Mixed substrates of pus of non-tuberculous origin and pus from mixed tuberculous empyema were studied *in vitro* with Pancreatic Dornase or trypsin added to them.[8] The effect of the enzymes was evaluated in the above study on the basis of the degree and rapidity of viscosity changes. In non-tuberculous pus Pancreatic Dornase was more effective than trypsin in producing pus lysis, causing it within the first minute of contact. Trypsin, which is a potent fibrinolysin, proved more effective than Pancreatic Dornase in lowering the viscosity of pus from mixed tuberculous empyema, which is rich in fibrinogen and fibrin.

Pancreatic Dornase exhibits some fibrinolytic activity, which is probably due to small amounts of trypsin and chymotrypsin.[14] These last-mentioned enzymes have in addition, mucolytic activity, which probably accounts for the effectiveness of Pancreatic Dornase on mucus and mucopurulent material.

Aerosolization and Pancreatic Dornase Activity.—Since many enzymes, including streptokinase and streptodornase, are known to be mechanically labile, this aspect of Pancreatic Dornase was tested by Reiser.[7] Employing a Vaponefrin glass nebulizer and 7 liters per minute oxygen flow he vaporized 5.0 cc of Pancreatic Dornase solution into an inverted beaker. The droplets that condensed on the walls of the equipment were collected. Pooled pus samples were mixed with this "nebulized Pancreatic Dornase" and with "non-nebulized Pancreatic Dornase" and the viscosity was then measured in one, five and fifteen-minute intervals and after twenty-four hours. The results in Figure 1 indicate that there was no significant change in the pus lytic activity of Pancreatic Dornase after aerosolization.

From the above pharmacological data it appears that Pancreatic Dornase has a specific effect against desoxyribonucleic acid and to a lesser degree against fibrin and mucus. This suggests that it may be of value in the treatment of processes where mucopurulent and viscous secretions are present.

Clinical Data.—The present study was undertaken to evaluate the efficacy of Pancreatic Dornase in the treatment of various broncho-pulmonary diseases. The preliminary laboratory and animal studies previously quoted have shown that Pancreatic Dornase is effective in liquefying mucopurulent exudates, that its action is not destroyed by aerosolization; it was also found that no toxic effects occurred with far higher doses than the estimated requirements for therapy.

Patients Treated.—In our present study Pancreatic Dornase aerosols were employed in the management of thirty-five patients with various pulmonary conditions: bronchiectasis, pulmonary abscess, pulmonary atelectasis, unresolved pneumonia, chronic bronchial asthma and emphysema. Most patients had in addition to the major chronic disease, one or more complicating processes (Table I.).

TABLE I. COMPLICATING PROCESSES FOUND IN THE THIRTY-FIVE PATIENTS TREATED WITH PANCREATIC DORNASE.

Primary Diagnosis	No. of Patients Treated	Emphysema	Fibrosis	Pneumonitis	Unresolved Pneumonia	Bronchial Asthma	Status Asthma	Cor Pulmonale	Right Heart Failure
Bronchiectasis	17	8	2	7	1	7	2	2	2
Bronchial Asthma	5	4		3			3	1	
Bronchitis	4	2		1		4		1	
Atelectasis	4								
Bronchial Pneumonia	3								
Emphysema	2			1					
Total	35	14	2	12	1	11	5	4	2

Methods of Administration.—The Vaponefrin nebulizer, which produces a fine mist of very small particles capable of penetrating the small bronchioles and alveoli, was used. Aerosolization was produced either by the pressure from a tank of oxygen through a standard pressure gauge, or by an intermittent positive pressure valve attached to a tank of oxygen. In the former, a Y-tube or similar button-like opening was inserted into the oxygen or air-feed line, so that thumb closure during inspiration would permit a continuous flow, whereas removal of the thumb during expiration would interrupt aerosol production.

For intermittent positive pressure on inspiration (IPPB/I), a Bennett valve was generally employed, set at an average pressure of 15 to 20 cm of water. This valve is an automatic, flow-sensitive cycling device. The patient completely controls the cycling of the valve by his own respiratory rhythm. The rate of instantaneous inspiratory flow, which may exceed 100 L/min, is of great advantage in the opening of the air passages and more efficient distribution of the drugs employed.[13]

The Pancreatic Dornase was mixed with a buffer solution (Sorensen) shortly before its administration. The solution thus prepared had a pH of 7.1.[14] Nebulization of Pancreatic Dornase by continuous flows of oxygen or air was given at 4 to 5 liters per minute flow. It was found that higher flows would cause foaming in the nebulizer and make treatment difficult.

Dosage.—After trying several dosage schedules, we found that 50,000 to 100,000 units of Pancreatic Dornase seemed to produce maximal benefit and could be repeated at six to eight-hour intervals without ill effects. In our series, one to three treatments daily were given depending on the severity and character of the case treated. A potent bronchodilator aerosol was added to the mixture, when bronchoconstriction was evident. The length of treatment was from two to six days until effects became apparent and maximal benefit was achieved, using clinical improvement, decrease in cough and volume of sputum, as criteria.

One or two twenty-four-hour sputum volumes were obtained as controls from each patient before treatment with Pancreatic Dornase. Sputum

volumes were then measured during the course of treatment and also after stopping therapy for at least two to three days. Frequent cytologic examinations of the sputum of each patient was made by Papanicolaou stains to detect possible metaplasia of cells which could be due to the treatment with Pancreatic Dornase.†

Results.—In practically all of the patients in our study beneficial effect was noted within one half to one hour after treatment. The cough became more effective and increasing amounts of sputum were expectorated in the following three to six hours. Twenty-four-hour-sputum volumes increased to two or three times the control volumes. At first, the sputum was thick and gelatinous. Gradually it was changed in character and became thin and milky in appearance. It soon lost its yellow and greenish color; a marked decrease in pus cells and cellular elements was subsequently noted microscopically.

Some patients noted subjective relief after the first treatment, and marked clinical improvement was generally noted after one or two days of treatment: in cases with fever, the temperature usually dropped to normal; cough was more productive than it had been previously, and secretions were expectorated with greater ease; the patients slept and felt better, and appetite and sense of taste improved, probably due to the decrease in cough and in the amount of sputum swallowed. In patients with chronic bronchial asthma and emphysema in status asthmaticus the sputum volumes were generally small prior to therapy, and there was a persistent wheeze and hacking nonproductive cough. Rapid improvement was generally noted after one or two treatments, probably due to the production of a more efficient cough mechanism which was productive of more copious sputum. In cases where a superimposed infection or pneumonitis was present, repeated treatment with Pancreatic Dornase appeared to speed the recovery process. The results in each patient are listed according to the disease process in Table II.

Discussion.—All of the thirty-five patients in our study appeared to benefit to some degree from the addition of Pancreatic Dornase to their therapy. The best results were obtained in those patients who had large amounts of tenacious mucopurulent secretions in the tracheobronchial tree, and in whom evacuation of these secretions was impeded. Included in this category were the patients with bronchiectasis, infected atelectasis, abscess and unresolved pneumonia.

Less striking results were obtained in the patients who had chronic asthma or emphysema as an underlying condition, with a superimposed infection putting them in status asthmaticus. These patients had a variable amount of obstructing secretions, which might account for the variability

†Studied at the Cytology Laboratory of the Mallory Institute of Pathology, Boston City Hospital.

TABLE II.

No.	Age	Sex	Diagnosis and History	No. Treatments	Days Treatment	Total Units Given	Results
			Bronchiectasis with:				
1	64	M	CPE, bilat. pneumonitis, dyspnea, orthopnea, cyanosis, purulent sputum. Hct 64%, Hgb 18 Gm T. 100-102°F.	6	3	600,000	Marked reduct. in sputum & cough; T. to normal; rapid recov. Addit. therapy: digitalis, aminophyllin, phlebotomy.
2	55	M	CPE, segmentectomy RLL, chr. hacking cough, dyspnea on exercise.	8*	4	400,000	Marked decr. in cough & ease in expectoration; feeling & sleeping better.
3	17	F	Recurr. infect., segmentectomy LLL, unresolv. pneumonia RLL, hacking nonprod. cough, small amt. purulent sputum. T. 101-10?°F.	9*	3	900,000	Quick resolution; T. to normal; good recovery in one week.
4	47	M	CPE, fibrosis, cor pulmonale, rt. heart fail., dyspnea, orthopnea, purulent sputum. T. 101°F.	6	3	300,000	Decr. in sputum viscosity; prompt improv. in cough; T. to normal. Addit. therapy: digitalis, aminophyllin, mercurials.
5	52	F	Recurr. infect., pneumonia RLL. T. 102°F.	8*	4	400,000	X-ray cleared promptly; T. to normal; general improvement.
6	48	F	CBA, bilat. pneumonitis, dyspnea. T. 101-10?°F. No response to ACTH & aminoph.	6*	3	700,000	X-ray showed clearing; thin sputum; less cough; no wheeze. T. to normal.
7	32	F	CBA, St. A., cyanosis, thick tenacious sputum & cough. No response to ACTH & aminoph.	8	4	400,000	General improvement; reduced cough; no wheeze; better expectoration.
8	37	F	CBA, dyspnea, pain rt. chest, severe cough. T. 102°F.	6	6	600,000	Less cough; thinning sputum; T. to normal.
9	63	M	CBA, CPE, dyspnea, tenacious sputum, unable to expectorate.	3*	3	300,000	General improvement; reduced cough and easy expectoration.
10	64	M	CBA, extensive fibrotic changes due to prob. active tbc., hacking nonprod. cough, mucopurulent & blood-streaked sputum. Low grade fever.	6*	5	700,000	Marked gen. improvement; T. to normal; reduced cough; thin sputum decr. in amt. with fewer cellular elements.
11	30	F	CBA, dyspnea, tenac. mucopur. sputum, severe cough. T. 101-10?°F.	10*	6	600,000	Immed. relief with easier breathing; gradual improvement; T. to normal.
12	33	F	CBA, St. A., pneumonitis LLL, severe cough; mucopurulent sputum. T. 102° F.	4*	4	400,000	Clearing of pneumonitis; better sleep; easier expectoration.
13	58	M	CPE, severe cough, dyspnea.	4*	3	300,000	Improvement after expectoration of large amt. of viscid sputum.
14	67	M	CPE, non-prod. cough, dyspnea, many rhonchi.	3	3	300,000	Marked improvement in cough and expectoration.
15	64	M	CPE, bilat. pneumonitis, dyspnea, cyanosis, rt. heart fail.	8	6	600,000	Clearing of pneumonitis; thin sputum expectorated with ease. Addit. therapy: digitalis, mercurials.
16	52	M	CPE, pneumonitis LLL, rt. heart fail., dyspnea, nonprod. cough.	6	6	600,000	General improvement; decreased cough; ease in expectoration. Addit. therapy: digitalis, mercurials.
17	75	M	C. B'chit. fract. rt. femur. Treated because of hacking cough interfering with sleep.	3	2	150,000	Expectoration of large amt. of sputum; comfortable and better sleep.
			Bronchial Asthma with:				
18	53	F	St. A. T. 101-10?°F. No response to ACTH & aminoph.	9*	3	450,000	Prompt improvement; decr. cough; T. to normal; comfortable.
19	30	F	St. A. of week's duration despite treatment, pain in chest, very uneomfortable. T. 10?°F.	8	4	400,000	Some improvement; less cough; T. to normal; comfortable.
20	42	M	Dyspnea, orthopnea, irritating cough.	3*	3	300,000	Immediate relief; less cough; very comfortable.

TABLE II—CONTINUED

No.	Age	Sex	Diagnosis and History	No. Treatments	Days Treatment	Total Units Given	Results
21	37	F	CPE, cor pulmonale, dyspnea for 3 d., cough, thick sputum, cyanosis. Hct 52%. T. 103°F.	6	3	600,000	General improvement; decr. cough; thin sputum; better sleep.
22	14	F	St. A. No response to aminoph., etc.	1	1	100,000	Immed. relief after expectorating 10 cc tenac. sputum; no wheeze.
			Bronchitis with:				
23	42	F	CBA, past pulm. tbc. with 10 rib thorocoplasty, cor pulmonale, pneumonia, decompensation, thick mucopurulent sputum. T. 100°F.	8*	4	400,000	Immed. improv.; easy expectoration; decr. cough. Addit. therapy: digitalis, aminoph., mercurials.
24	42	F	CBA, dyspnea. T. 101°F.	3	2	150,000	Easier expectoration; comfortable.
25	62	M	CPE, CBA, dyspnea, cyanosis, non-prod. cough interfering with sleep.	4*	2	200,000	Improved remarkably; less cough; better sleep.
26	63	F	CBA, CPE, fract. hip, sev. cough, difficult expectoration.	2	2	200,000	Decr. cough; thin sputum; comfortable.
			Atelectasis				
27	62	M	Atelectasis RLL & RML following fract. ribs and concussion, unable to cough, aspiration unsuccessful.	4	2	400,000	Sputum thin & aspirated easily. Death due to cerebral lesion.
28	32	F	Atelectasis of post. segm. RUL, probable abscess, non-prod. irrit. cough, small amt. bld. tinged purulent sputum. T. 102-104° F.	8*	4	600,000	Clearing lung segments; expect. large amt. bld. tinged purulent sputum; X-ray showed clearing.
29	47	M	Post-op. atelectasis of LUL.	2	2	200,000	X-ray showed clearing on 2nd day of treatment.
30	47	M	Atelectasis RLL, traumatic fract. of several ribs, pt. unable to cough effectively because of pain.	3	3	300,000	Clearing of atelectasis by X-ray on 3rd day of therapy.
			Bronchopneumonia				
31	60	M	Adm. with skull fract., partial remov. of rt. hemisphere of brain, coma, large amt. sputum in tracheobronchial tree, aspirations ineffective.	8	4	800,000	Lge. amt. thin sputum aspirated following treatment; improved respiration.
32	82	M	Bilat. bronchopneumonia, cough inhibited by chest pain, bld. tinged purulent sputum. T. 102°F.	6	5	600,000	X-ray showed clearing; general improvement; T. to normal.
33	72	M	Bilat. bronchopneumonia, cough, small amt. sputum. T. 102°F.	6	6	600,000	X-ray showed clearing; general improvement; T. to normal.
			Chronic Pulmonary Emphysema with:				
34	60	M	Fibrosis, bilat. pneumonia, cyanosis, severe wheeze, non-prod. cough, small amt. purulent sputum. T. 100-102°F.	10*	5	500,000	Easier expectoration; sputum thin & incr. in volume; T. to normal. Addit. therapy: digitalis, antibiotics.
35	64	M	Fibrosis, irrit. cough, dyspnea on exercise, unable to sleep, thick mucopurulent sputum.	4*	4	400,000	Less cough; decr. dyspnea; better sleep.

*Use of IPPB/I for administration of Pancreatic Dornase aerosol.

Abbreviations:

CBA	Chronic Bronchial Asthma
C. B'chit.	Chronic Bronchitis
CPE	Chronic Pulmonary Emphysema
St. A.	Status Asthmaticus
Hct.	Hematocrit

in results. Those in whom this factor was great would be expected to improve following the liquefaction of their sputum, while those in whom this factor was small, would not.

It is much more difficult to evaluate a therapeutic adjuvant which is used only in conjunction with many other forms of treatment than it is to assess the benefit of a therapeutic agent that can be used alone. In our study on Pancreatic Dornase, it was not used as the only treatment in any case, and it cannot be held responsible for a single "cure." The objective evidence of effect of Pancreatic Dornase administration lay in the invariable decrease in viscosity and increase in volume of the patient's sputum following its use. It was our impression that the patients receiving it improved more rapidly and uniformly than they would have otherwise.

One half of the patients in our study received the aerosol of Pancreatic Dornase administered simultaneously with intermittent positive pressure breathing (IPPB/I), using the Bennett valve, while the other half received it with the Vaponefrin nebulizer and constant oxygen flow technique. It appeared to us that better results were obtained with the combined aerosol-intermittent positive pressure breathing technique. The latter technique provides more complete ventilation of the lungs and hence more complete distribution of the enzyme to poorly aerated segments. The asthmatic patients, especially, seemed to tolerate the fifteen-to-twenty-minute aerosol treatment better when it was given with the Bennett valve apparatus.

We did not observe any of the side effects with Pancreatic Dornase that were previously reported with Tryptar aerosol,[18,19] such as hoarseness, and eyelid or nasal irritation. Actually, we observed no side effects in our small series of patients, either during or after treatment. Nevertheless, because of the protein nature of Pancreatic Dornase, allergic reactions may possibly occur in allergic or previously sensitized subjects. The cytologic studies (Papanicolaou stains) on the sputum of each patient treated were reported negative for evidence of metaplasia. These studies were made following the report of Farber of cellular metaplasia observed in the sputum of patients treated with Tryptar aerosol.[3]

Pancreatic Dornase appears as a safe and most helpful adjuvant in the therapy of bronchopulmonary diseases where tenacious, mucopurulent secretions constitute a major factor in the pathologic process, and evacuation of the secretions is of utmost importance.

SUMMARY

1. Thirty-five patients with chronic bronchial asthma, chronic pulmonary emphysema, bronchiectasis, lung abscess, pneumonia and atelectasis were treated with aerosols of Pancreatic Dornase.

2. The Pancreatic Dornase was administered in 50,000 to 100,000 units per treatment, one to three treatments daily for one to six days.

3. The Pancreatic Dornase was aerosolized with the direct Vaponefrin

nebulizer-oxygen flow technique or by intermittent positive pressure breathing with the Bennett valve. Treatment with the latter technique appeared more effective.

4. Pancreatic Dornase aerosols appeared to be a safe and useful aid in the evacuation of viscous, tenacious, mucopurulent secretions. Its effect varied from good to excellent depending upon the nature of the underlying disease.

5. No side reactions due to treatment with Pancreatic Dornase were observed in our series of thirty-five patients.

NOTE: Since submitting this paper, an additional twenty-six patients with similar pathology have been treated with Pancreatic Dornase. The results were the same as described and no toxicity was observed.

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CLINICAL EVALUATION OF DIPHENYLPYRALINE IN RAGWEED POLLINOSIS

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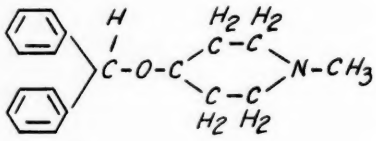
DESPITE the growing list of antihistaminic drugs, the search goes on for an antihistamine of greater potency, wider effectiveness, productive of fewer side reactions. Diphenylpyraline, synthesized by Nopco chemists in 1949, was demonstrated to have a high antihistamine activity and a very low toxicity in laboratory animals. A preliminary report of its therapeutic usefulness indicated its value.[1,2] A clinical evaluation of the drug was, therefore, undertaken during the 1953 ragweed season.

Diphenylpyraline represents an entirely new class of antihistamines with the structural formula



Its chemical name is 1-methyl-piperidyl 1-4 benzhydryl ether and its properties are quite different from those of other antihistamines containing the benzhydryl ether group.

One hundred ragweed hay fever patients were given this drug either as sole or adjunct therapy during the 1953 ragweed season. Table I represents an analysis of these patients. Ages ranged from three to seventy-three; the sexes were almost evenly divided; the duration of hay fever varied from one to forty seasons. There were twenty-two patients with first manifestations of hay fever. Of the remaining seventy-eight all had had previous treatment. Results of this treatment are noted in Table I. Sixty-two of this group had no associated allergic conditions while thirty-eight manifested with at least one major associated condition.

Because the twenty-two patients with first hay fever symptoms were seen too late to be given effective hyposensitization, they were placed on diphenylpyraline as the sole therapeutic agent (Table II). The dosage varied from 1 to 4 mgm four times a day, the average requirement being 2 mgm three times a day. Dosage was maintained from the first day the patient was seen until the end of the ragweed season. This varied from twenty to forty-two days. There were two patients who seemed to develop a mild tolerance to the drug necessitating an increase in dosage, in one from 1 mgm b.i.d. to 2 mgm t.i.d. and another from 2 mgm t.i.d. to 2 mgm q.i.d. A third case had relief at each increase but soon experienced return of symptoms Since in the first two cases increasing the dose occurred early in administration of the drug and full effectiveness was obtained

TABLE I. TREATMENT OF RAGWEED HAY FEVER WITH DPP
One Hundred Patients

Age Group	No. Patients	Sex		First Season	Max. Seasons	Simple H.F.	Number and Type Complications										Type and Results Previous Treatment						Remarks
		M	F				Asthma	P.A.C.	Hives	A.N. Edema	Eczema	G.I. Allergy	Bronchitis	Migraine	Eye Allergy	Total	Specific Only	Results	Adjunct Only	Results	Specific and Adjunct	Results	
3–10	15	10	5	5	5	9	1		2		1		1	1		6	4	2 Good 2 Poor	4	1 Good 3 Poor	2	2 Good	
10–20	12	6	6	3	9	7	1					2	1	1		5	3	1 Excell. 1 Good 1 Poor	5	5 Poor	1	1 Good	
20–30	20	8	12	3	20	12	1	4		1		1	1			8	6	1 Excell. 5 Good	7	2 Good 5 Poor	4	1 Excell. 3 Good	
30–40	30	13	17	8	30	21	1	3				2		1	2	9	10	6 Good 4 Poor	6	1 Good 5 Poor	6	2 Excell. 3 Good 1 Poor	
40–50	10	4	6	2	36	5	2	3								5	4	3 Good 1 Poor	2	2 Poor	2	1 Excell. 1 Poor	
50–60	8	5	3	1	40	6	1	1						1		3	1	1 Poor	4	1 Good 3 Poor	2	1 Good 1 Poor	
60–70	4	2	2	0	31	2	1	1								2	1	1 Good	2	2 Poor	1	1 Good	
70–80	1		1	0	10	0										0			1	1 Good			This patient was 73 with Rx for past 5 years limited to antihistamines
Totals	100	48	52	22		62	8	12	2	1	1	5	3	4	2	38	29		31		18		

TABLE II. TREATMENT OF HAY FEVER WITH DPP ONLY (GROUP I.)

Twenty-two Patients With First Symptoms

No.	Age	Sex	Associated Allergy	Dosage in mgm.	Days Rx	Results	Tolerance	Side Effects	Placebo Days	Remarks
1	3	M	Hives	1 B.I.D.	34	Excellent	—		Severe H.F. & Hives	Hives controlled by DPP also
2	3	F		1 B.I.D.	34	Excellent	—		Severe H.F.	
3	8	F		2 B.I.D.	30	Excellent	—	Dry mouth	Moderate H.F.	
4	9	M	Eczema	2 T.I.D.	28	Excellent	—		Moderate H.F.	Eczema unaffected by DPP
5	9	M		2 T.I.D.	29	Good	Dose increased from 1 mgm. B.I.D.		Severe H.F.	
6	13	F	G.I. Allergy	2 T.I.D.	20	Good	—		Severe H.F.	G.I. symptoms controlled by DPP
7	18	M		2 T.I.D.	40	Excellent	—	Headache	Moderate H.F.	Headaches mild
8	18	M		2 q.I.D.	42	Good	—		Moderate H.F.	
9	22	F		2 q.I.D.	38	Excellent	Dose increased from 2 mgm. B.I.D.		Severe H.F.	
10	26	M		2 T.I.D.	28	Excellent	—		Severe H.F.	
11	28	F		4 T.I.D.	22	Good	—	Dry mouth & eyes	Moderate H.F.	Side effect similar to atropine effects blurring
12	32	M	P.A.C.	4 B.I.D.	32	Good	—		Severe H.F.	
13	34	F		2 B.I.D.	40	Excellent	—		Severe H.F.	
14	35	M	A.N. Edema	2 T.I.D.	39	Excellent	—		Severe H.F.	
15	35	F	P.A.C.	2 T.I.D.	26	Excellent	—		Severe H.F.	
16	38	F		2 q.I.D.	40	Good	—		Severe H.F.	
17	38	M	P.A.C.	4 q.I.D.	32	Poor	Each increase—good results, then 0		No change	Multiple bilateral nasal polyps
18	38	F		2 B.I.D.	40	Excellent	—	Parching	Severe H.F.	
19	39	M	Asthma	4 q.I.D.	42	Poor	—		No change	Asthma unaffected by DPP
20	44	M		2 q.I.D.	38	Excellent	—		Severe H.F.	
21	45	M		2 q.I.D.	36	Excellent	—		Severe H.F.	
22	57	F	P.A.C.	4 T.I.D.	40	Good	—		Severe H.F.	

TABLE III. TREATMENT OF HAY FEVER WITH DPP AS ADJUNCT TO HYPOSENSITIZATION (GROUP II.)
Seventy-Eight Patients

Type of Case	IIA Simple Hay Fever	IIB Hay Fever with Associated Allergic Conditions
No. Patients	29	49
Use of DPP	As needed throughout season	As needed throughout season
Dose Range	2-4 mgm. q4h PRN	2-8 mgm. q4h PRN
Average Time Lapse for Relief	5—30′	5—40′
Duration of Effect	2-10 Hrs.	½-8 Hrs.
Number with Tolerance	1	2
Side Effects	3 Parching, 1 Headache	4 Parching
Patients with No Effect	2	7
Placebo Effect	None	None
Remarks	Side effects mild	Asthma and severe pal unaffected by drug

thereafter, it is questionable whether or not these represent true instances of tolerance.

The results in percentage are indicated in Table IV, Group I. It is interesting to note that where hives or gastrointestinal allergy were associated with hay fever, these, too, were controlled by the drug. Eczema, asthma, and nasal polyps however, in the three individuals in whom these were present, did not yield. The drug was without effect in two patients in this group, one of whom had severe asthma, the other multiple nasal polyps in addition to hay fever.

Side effects occurred in four of these twenty-two patients and consisted of dryness of the mouth in three, and mild headache in one. One of the three with dryness of the mouth also experienced dryness of the eyes without, however, blurring of vision. In none of these cases were the side effects severe enough to necessitate stopping the drug.

Placebos, identical in appearance with the drug-containing tablet, were given all of these patients one day per week throughout the season, the day being varied from week to week. Without exception, those patients being benefited by diphenylpyraline experienced severe symptoms on these days. See Table II.

Table III tabulates the various factors in Group II consisting of the remaining seventy-eight patients. Generally, this group was divided into IIa and IIb, the first representing those patients without associated allergic conditions, the last those patients with associated allergic conditions. All in Group II were receiving hyposensitization in addition to diphenylpyraline, and all had received treatment in the past and thus could serve as controls for themselves. The entire group was instructed to take the drug only if symptoms appeared. Group IIa, simple hay fever, varied in its dosage from 2 to 4 mgm every four hours during times of symptoms and reported effectiveness within five to thirty minutes of taking the drug. A single dose relieved for two to ten hours. Only one patient showed what seemed to be tolerance requiring an increase in dosage to 4 mgm every two hours. The drug was ineffective in two of this group; other antihistamines tried were also ineffective. Three of this group experienced parching as a side-effect and one, headache. Placebos were given this

TABLE IV. RESULTS OF TREATMENT WITH DPP

Patient Group	Percent Effective	Percent Ineffective	Percent Side Effects	Remarks
Total Patients—100	89.0	11.0	12.0	
Group I—22 Patients First hay fever season DPP taken throughout season, daily—No other treatment	90.9	9.1	18.1	In no case were the side effects of great enough severity to necessitate cessation of the drug
Group II—78 Patients Hay fever—2 or more seasons. Rx—DPP and hyposensitization	88.4	11.6	10.3	
Group IIA—29 Patients Simple hay fever	93.1	6.9	13.8	
Group IIB—49 Patients Hay fever and associated allergy	85.7	14.3	8.2	

group from time to time and were reported ineffective.

In Group IIb, with associated allergic conditions, a higher dosage was required for effectiveness and a percentage reported a longer time lapse between taking the drug and relief of symptoms. Generally, the duration of beneficial effect from the drug was shorter in this group and two instances of what seemed to be tolerance were reported. In these latter, 8 mgm of the drug finally had to be taken and at this level effectiveness continued. Parching, of no great moment, was noted as side effects in four patients. Seven of this group were not benefited by the drug. Of these seven, all had marked asthma or severe perennial allergic coryza associated with hay fever. Placebos yielded beneficial results in no case.

Table IV tabulates the percentage results and side-effects in the total group and its subdivisions.

COMMENT

It must be stressed that this investigation represents a clinical evaluation of a specific drug. Although controls were used in the form of placebos, no comparison studies with other antihistamines were run during the same period. Nonetheless, the unusual severity of the 1953 ragweed hay fever season in New York served to make exceptional demands upon the effectiveness of the drug. The opportunity to restrict therapy to the drug alone in the group of patients with first hay fever symptoms was invaluable in observing tolerance. With these conditions in mind, general conclusions can be made as listed below.

CONCLUSIONS

1. Diphenylpyraline is an effective antihistamine drug for uncomplicated hay fever.
2. Effectiveness is reduced in hay fever associated with severe respiratory allergy.
3. Dosage averages 2 to 4 mgm t.i.d.
4. Side-effects seem to be minor and, in this group of patients, were of no great inconvenience.

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CORTOGEN NASAL SUSPENSION WITH CHLOR-TRIMETON IN THE TREATMENT OF ALLERGIC RHINITIS

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THIS STUDY was designed to determine the efficacy of an antihistamine-cortisone preparation in the treatment of allergic rhinitis. Allergies are the conditions most commonly affecting the mucous membranes of the nasal passages and the paranasal sinuses.[13] In the treatment of allergic rhinitis, consideration must be given to the medical, surgical, and immunologic approaches. It was recognized that the medication used is palliative rather than curative. However, its investigation was undertaken because of realization of the need for a more effective palliative for this widespread condition.

In a previous study,[9] Chlor-Trimeton 0.25 per cent by intranasal application proved highly satisfactory as a vasoconstrictor in patients with allergic rhinitis. The results are shown in the accompanying table. This particular antihistamine was chosen because its therapeutic effectiveness has been reported to be high, whereas the side actions associated with its use are probably fewer than those noted with other antihistamines.[1,2,6,7,8,10,11,12]

Among the gratifying results obtained with cortisone have been those in conditions in which its local use is possible. In such disorders, the dose of medication is small and systemic manifestations are absent. The local use of cortisone in the treatment of severe allergic conditions of the eye, as well as ocular inflammations, has proved the activity of the steroid when applied topically. Bordley[3] reported encouraging results with cortisone as a nose drop, and Dill and Bolstad[4] reported satisfactory relief of symptoms of allergic rhinitis using cortisone in a nasal spray. Fabricant[5] reported a slow but definite regression of nasal polyps with the use of a cortisone nasal spray.

It seemed logical to assume that utilization of the marked vasoconstricting property of Chlor-Trimeton in an aqueous vehicle would facilitate the application of cortisone to the nasal mucosa. Observations on this premise and an extension of previous studies were carried out using a new combined suspension-solution of these two drugs. This preparation will be referred to as "Cortogen Nasal Suspension with Chlor-Trimeton."* This is a microcrystalline suspension of cortisone acetate 0.5 per cent in a 0.25 per cent solution of Chlor-Trimeton (chlorprophenpyridamine maleate). A clinical evaluation of this nasal preparation in 153 patients with positive diagnoses of allergic rhinitis is given in this report. The diagnosis was

*Supplied by the Division of Clinical Research, Schering Corporation, Bloomfield, New Jersey. Cortogen and Chlor-Trimeton are registered trademarks for cortisone acetate and chlorprophenpyridamine maleate, respectively.

TABLE I. RESULTS WITH "CORTOGEN NASAL SUSPENSION WITH CHLOR-TRIMETON," AND A COMPARISON WITH CHLOR-TRIMETON SOLUTION ALONE

Preparation	No. of Cases	No Relief	Fair Relief	Good to Excellent Relief	Total Response
Chlorprophenpyridamine maleate* solution 0.25%	61	6 (9.8%)	7 (11.5%)	48 (78.7%)	55 (90.2%)
Cortogen Nasal Suspension 0.5% with Chlor-Trimeton 0.25%	153	11 (7.2%)	10 (6.5%)	132 (86.3%)	142 (92.8%)

*Chlor-Trimeton Maleate

established in each case by the presence of edematous mucous membranes and watery secretions with confirmation by skin testing. One hundred and thirty-eight patients proved to be sensitive to pollens. In them the nasal discharge was profuse during the pollen season. The remaining fifteen patients gave positive reactions to skin tests with extracts of various inhalant allergens.

DISCUSSION

Selection of Patients.—There were one hundred and fifty-three patients in this study, ranging in age from four to fifty-four years, the majority being in their third decade. Fifty-five were children who ranged in age from four to fifteen years. The 138 patients with seasonal allergic rhinitis were observed during the local 1952 pollen season. Among these patients, and the fifteen with perennial allergic rhinitis, were some previously responding to antihistamine tablets, some who did not, and some who had received no previous oral antihistamine therapy. The patients in this study received only the "Cortogen Nasal Suspension with Chlor-Trimeton" as a therapeutic aid in the treatment of their allergic rhinitis, no systemic medication being employed.

Dosage and Procedure.—In the office, three drops of the suspension-solution were instilled into each nostril. The patients were instructed to hold their heads back to instill the solution and then to lower their heads between their knees for two minutes following instillation. This procedure was to be repeated at home every four hours, or less frequently as necessary. No patient was included in this study who did not use the nasal preparation for a minimum of two weeks. The period of administration was two weeks to one month in seventy-six patients, one to six months in sixty-one, and six to twelve months in sixteen.

The first instillation of the preparation was followed by direct observation of the nasal mucosa to determine the time of onset and degree of vasoconstriction. In practically all instances vasoconstrictive action was observed after a few seconds to within five minutes. Subsequently, on further office visits, the nasal mucosa was carefully observed and the patients thoroughly questioned concerning the degree and duration of relief experienced.

Evaluation of Results.—The results are summarized in the table. Among the 153 patients receiving this suspension, eleven (7.2 per cent) obtained no vasoconstrictive effect on the nasal mucosa; ten (6.5 per cent) showed slight to moderate vasocontriction which lasted two hours or less; 132 (86.3 per cent) exhibited moderate to complete vasoconstriction which lasted three to six hours or longer; nine claimed relief from twelve to twenty-four hours following instillation of the drops. Generally, the patients stated that their nostrils cleared in from two to five minutes and the action lasted from two to twelve hours.

Side Reactions.—No side reactions were encountered that necessitated the alteration or discontinuance of therapy. No systemic effect or latent irritation of the nasal mucosa was observed or reported. Approximately one-half of the patients developed temporary partial anaesthesia of their nasal mucosa. About 25 per cent of the patients complained of a mild transitory stinging sensation when the drops were instilled. About 20 per cent of the patients mentioned that they experienced dryness of the posterior nasopharynx following instillation of the preparation. It was noted that marked anaesthesia of the nasal mucosa was evident in a fifty-four-year-old woman. This observation was also true in a forty-five-year-old man who complained of marked irritation of the posterior nasopharynx. However, Chlor-Trimeton Solution 0.25 per cent alone induced the same sensation as "Cortogen Nasal Suspension with Chlor-Trimeton." In the case of a nine-year-old child, there were signs of rebound swelling. This phenomenon was not observed in a single case in the study employing Chlor-Trimeton 0.25 per cent alone.[9] There were no signs of sodium and fluid retention as evidenced by stable body weights and normal urinalyses. (None of the patients had been placed on sodium-free diets.) No complaints of weakness or cardiac palpitation were noted to indicate toxic systemic effects of the active ingredients.

SUMMARY

One hundred and fifty-three patients varying in age from four to fifty-four years with positive diagnoses of allergic rhinitis, received "Cortogen Nasal Suspension with Chlor-Trimeton" as a topical nose drop. One hundred and forty-two patients (92.8 per cent) showed varying degrees of response to this treatment. One hundred and thirty-two (86.3 per cent) obtained good to excellent relief of symptoms. Only 10 (6.5 per cent) showed a response which was considered fair. Eleven patients (7.2 per cent) obtained no relief.

A comparison of these data with those obtained using the antihistamine alone indicates greater therapeutic effectiveness with the combined therapy. The rebound phenomenon commonly encountered with the prolonged use of other types of vasoconstrictors was seen in only one patient (0.6 per cent). Patients continued to respond favorably to the vasoconstricting

action of this preparation when applied to the nasal mucosa for several months, indicating that tolerance to the preparation was not developing. No systemic side reactions were encountered during this study.

CONCLUSIONS

1. "Cortogen Nasal Suspension with Chlor-Trimeton" (cortisone acetate 0.5 per cent with chlorprophenpyridamine maleate 0.25 per cent) is safe for intranasal administration and is equally well tolerated in adults and children.

2. Prolonged usage of it is without systemic manifestations.

3. Local reactions to application of the medication are usually transitory and mild.

4. This preparation provides rapid and prolonged vasoconstriction of the nasal mucosa of patients with allergic rhinitis.

5. This study showed no "drug fast" subjects and a remarkable absence of the "rebound phenomenon."

6. The therapeutic effectiveness of "Cortogen Nasal Suspension with Chlor-Trimeton" observed in this study was of a very high order making it a preparation of choice for patients with allergic rhinitis.

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ASTHMA PRODUCED BY IPECAC

(Historical Document)

ASHBEL PATTERSON, M.D.

TO THE EDITOR OF *THE BOSTON MEDICAL AND SURGICAL JOURNAL.*

Sir,—I have observed in a late number of your Journal, a communication from Uriah Turner, M.D., entitled "Asthma caused by Ipecacuanha," illustrated by his own case, in which he observes that "he has reason to believe that these effects are new to a majority of the profession." Having for a long series of years suffered most severely in a similar manner from these singular effects of ipecac, and having made them the subject of long and anxious reflection, I take the liberty of forwarding to you a brief statement of my experience and observation on this singular, and to me painful, subject.

Yours respectfully,
ASHBEL PATTERSON

Homer, N. Y., Dec., 1843.

I HAVE BEEN to some extent a dyspeptic from early life, but had not supposed there was a strong predisposition to disease of the respiratory organs. When about twenty years of age I had a catarrhal affection, which has so far impaired the sense of smell, that up to this time (a period of more than twenty years) I have not been able to perceive odors unless they were decidedly pungent. At the age of twenty-five, I observed that I was subject to occasional paroxysms of sneezing: the attacks were sudden, and the convulsive effort was often painfully violent. Occasionally these paroxysms were accompanied with dyspnoea or suffocating sense of stricture at the chest, and a most distressing oppression at the precordia—and were always preceded by, and accompanied with, a most harassing titillation of the nostrils, and at times with nausea, and convulsive, but ineffectual efforts to vomit.

For a long time I was unable to account to myself for this singular and distressing state of affairs. At length, after having prepared an emetic of ipecac, mixed it myself, and administered it to a patient, I was attacked with the whole concourse of symptoms enumerated above. Each one was marked by peculiar violence. In a very short time, probably ten or fifteen minutes, I found myself laboring under a severe and convulsive paroxysm of asthma; the danger of suffocation seemed imminent in the extreme. I sought relief in the open air. During my ride home, the oft-repeated and convulsive paroxysms of sneezing were almost sufficient to throw me from my saddle. These symptoms, like other similar attacks, lasted about two hours, and gradually subsided, with cough and expectoration.

It was during this paroxysm that the idea first suggested itself to my mind that these singular attacks were produced by inhaling the powder of ipecac. I taxed my memory in regard to previous asthmatic attacks, and I could recollect no instance of their occurrence without a previous exposure to the influence of this, to me, extraordinary agent. The idea was to me entirely new; but the sad recollection of previous exposures and suffering, convinced me that the idea, however novel, was nevertheless true.

I have since used many precautions to avoid its deleterious effects; but the constantly recurring necessity for its use, in a country practice, has

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given me too many opportunities of testing, by painful experience in my own person, the potency of its influence in exciting asthma in a class of constitutions of peculiar idiosyncrasy. For a long time I supposed that inhaling the powder was necessary to produce these effects; but I have since learned that swallowing it in tincture or infusion will produce similar but not as violent results.

It is astonishing, I had almost said incredible, how small a quantity of ipecac, inhaled, will produce the most sudden and violent paroxysms. About four years since, a clerk in my drug-store scattered a small quantity of ipecac, on the counter, which he brushed off with a counter-brush; the doors and windows were open, and a current of air had passed through the store for half an hour before I entered it; in two minutes after my arrival, I was seized with a violent sneezing, followed almost immediately with a paroxysm of asthma which entirely disabled me for the day. But a few days since, a young man in my office was directed to transfer a quantity of ipecac from a paper to a jar. I left the office for half an hour. On my return I was almost instantly attacked with one of the most fearful paroxysms that I have ever experienced; the extreme sense of suffocation, oppression at the precordia, a most withering and exhausting nausea, convulsive but totally ineffectual efforts to vomit, attended with simultaneous spasms of the diaphragm and muscles of the chest and abdomen, produced altogether a state of suffering which defies description. In each of these instances the quantity of ipecac inhaled must have been infinitely small.

That these effects of ipecac do not depend invariably on the irritating properties of the powder when inhaled, but on idiosyncrasy, seems to be established by the following circumstances. In the summer of 1841 I had a long course of bilious fever. The attack was marked by no particular symptom of disease of the lungs; but as soon as I commenced the use of ipecac or Dover's powder as a febrifuge, I had a convulsive and harrassing cough and dyspnoea; every effort to speak was interrupted by a spasm of the muscles of respiration; and a sense of sinking and oppression of the precordia, which constituted, in my opinion, the climax of human suffering. For a long time the agency of ipecac in producing these symptoms was not suspected (as the utmost care was taken to prevent my inhaling the powder; but they continued with unabated violence, until I discontinued the use of ipecac in every form.

The predisposition to asthma was unquestionably produced by the early catarrhal affection to which I have alluded; and its ultimate development depended entirely upon long-continued and repeated exposures to the influence of ipecac; but when this predisposition had become established, other exciting causes would produce a paroxysm, but no cause has yet excited such violent symptoms as ipecac.

A peculiar state of the atmosphere will produce it, and a long continuance of this state will cause it to return periodically. The month of October, 1842, was one of the most pleasant months of the season; the days were sunny and the air mild; the nights were cloudless; but from the numerous streams in this valley there rose a dense fog which hung upon their banks until a late hour in the morning. Exposure to or inhaling this fog invariably caused a paroxysm of asthma, which lasted two or three hours, and terminated with cough and expectoration. After a few exposures to these fogs, the attacks became periodical, making their onsets with singular exactness, invariably within twenty minutes of 4 o'clock in the

morning, waking me from refreshing sleep to undergo all that is dreadful in this most suffocating affection. These paroxysms were so severe as to render a recumbent posture insupportable; but they were in a great degree free from that sense of sinking, nausea and spasm, which accompanied those caused directly by ipecac. These diurnal paroxysms continued without a single intermission until the seventh of November, when a violent storm of rain, sleet and snow wrought an entire change in the state of the atmosphere, when they suddenly ceased. Thus

"Chill November's surly blast"

operated as a charm in relieving me from attacks, which from their uniformity and severity rendered life almost a burthen. In this respect, as well as in many others, there seems to be an essential difference between ordinary asthma and that form of the disease produced by ipecac. It might be interesting to trace out and define these points of difference; but having extended this communication already to too great a length, I shall leave its further consideration for some future occasion.

AMERICAN FOUNDATION FOR ALLERGIC DISEASES

A very favorable response to the appeal to allergists in the American Academy of Allergy and the American College of Allergists has been reported by Mr. Reuel Estill, Public Relations Director. There is reason to believe that the anticipated quota to be donated by the allergists for the first year in establishing the Foundation, before lay members and subscriptions are solicited, will be reached. The first folder, made up in question and answer form by a competent committee of allergists, giving cogent and pertinent information to allergy patients and laymen interested in allergies for distribution in doctors' offices and for mailing purposes, has been issued. The Executive Committee of the Board of Trustees met at Houston before the meeting of the joint committee of the Academy and the College and accepted the report of Mr. Estill. Besides individual contributions, the Academy has given $5,000.00, which was the sum agreed upon by officers of the Academy and the College as a collective contribution for each society. There was a special assessment of $6.00 to Active and Associate Fellows of the College residing in this country to meet the unpaid balance. There remain 275 members who should meet this assessment obligation before the annual meeting in April. Please remit now, if you have not done so.

Progress in Allergy

HAY FEVER

A Review of the Literature of 1952

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FOREWORD

The year of 1952 has certainly been no exception in the plethora of articles dealing with allergy. However, we do not seem to be any closer to the understanding of the basic features underlying the allergic diathesis. This year we have some additional information in regard to the use of ACTH and Cortisone in relation to hay fever. Much work is in progress in an attempt to find a single pure antigen and, as of this writing, we might almost express optimism in this regard.

IMMUNOLOGICAL INVESTIGATIONS

R. Friedmann[54] has compiled a most comprehensive bibliography on the chemical and immunological properties of timothy grass and pollen extracts. In this paper, she correlates the present knowledge of all pollen extracts with some of her own investigations. The problems which we are confronted with, in standardization of pollen extracts, is discussed and everyone interested in this subject should read this very important article.

Malkiel and Feinberg[105] studied neutralizing antibodies in non-allergic individuals by the following method: They performed neutralizing antibody titrations in a series of non-atopic volunteers receiving one of the following ragweed preparations: (1) aqueous, (2) dialyzed aqueous, (3) alum precipitated, (4) tannic acid precipitated extract. Extracts of the following were also studied; 10 per cent polyvinylpyrrolidone, pertussis vaccine, and 2 per cent sodium gentisate. A total of over 370,000 protein nitrogen units of ragweed extract was administered during the course of twenty-six weekly injections. No significant increase in neutralizing antibodies was detected after such a series of injections.

Menzel, Kessler et al,[111] in their immunoserologic studies of the immediate wheal-type allergies, report that the skin sensitizing antibody for ragweed has not yet been found to exist in the albumin or Alpha I components of serum. It appears to exist in gamma globulin, but with variations. It appears to exist in the beta and possibly the Alpha II globulin or the interzones to these components. Neither gamma globulin nor beta globulin nor Alpha II is essential to skin reactivity since reactions have been found in the absence of each of these components in electrophoretically detected amounts. The differences observed in different sera suggest a variation in the distribution of the sensitizing antibody through the globulin area and in this way agrees with the biological variations that regweed sensitive sera have been shown to possess.

Vaughan, Favour, and Jaffee,[178] in their study of the partition of the skin-sensitizing antibody among alcohol-fractionated plasma proteins, note

that the skin-sensitizing antibody of ragweed hay fever has been shown to be concentrated among the proteins of Fraction IIId, as separated by alcohol precipitation in the cold.

Hoet, Mynors,[75] *et al*, in their serological studies on pollen extracts, demonstrated the specificity of the antigenic mosaic of pollen extracts and estimated the relative strength of the serological reactive components in these extracts by means of inhibition tests.

Perlman,[122] in a study involving chromatographic analysis of ragweed pollen extracts, found that when crude giant ragweed pollen extracts were subjected to chromatographic studies, the substances eluted following application of various reagents to the paper, and then studied by scratch tests for antigenic potency, showed the presence of large number of components in the crude pollen extract, and that at least two of them produced positive skin reactions when tested in susceptible individuals.

Matheson, Nierenberg, and Greengard[106] studied the skin reactivity of the newborn. They showed that the skin of the newborn contains fixed tissue antibodies.

Baldwin's[12] investigation of the biochemical aspects of nasal polyps for H_2O, chlorides, sodium, potassium, calcium, magnesium, and total nitrogen revealed that the sodium-chloride ratio was similar to blood.

Berdal[14] studied edematous fluid squeezed from nasal polyps, serum from a cantharides bulla, and blood serum by passive transfer tests. He found positive reactions at 1:2000 dilutions of polyp fluid; 1:10 bulla fluid, 1:100 in the serum using mixed house dust, foxtail, grass, and milk as the allergens. He concluded that in some cases of nasal polyps, an accumulation of specific antibodies against certain definite allergens may be found in edematous polyps fluid as compared with cantharides bulla and blood serum.

Rappaport, Samter, Catchpole, *et al.*,[132,133] revealed that by biopsy studies made of the middle turbinates of patients sensitive to ragweed, as compared with nonsensitive individuals, showed a decrease in the intensity of the staining of the ground substance, as well as in the width and staining intensity of the subepithelial, perivascular, and periglandular mucous membranes. Such changes were also seen in the interepithelial cement substances, and the zymogen granules of the mucous glands, and are believed caused by increased depolymerization of the ground substance.

POLLEN

We feel that pollen surveys contribute greatly to the accurate diagnosis and treatment of pollenosis. We urge that a continued effort be expended in this direction. The pollen survey committee of the American Academy of Allergy and the aerobiology[25,26] committee of the American College of Allergists are working along these lines and their reports should prove very interesting. The pollen survey committee of the American Academy of Allergy[5,6,7,9] reported for the year of 1952, from seventy stations in the United States, Canada, and Mexico. From each station, the total counts for each of the important tree, grass, and weed pollen are reported for each month and for the year.

Copies of the 1952 edition of the booklet[9] containing all available ragweed pollen indexes for communities in North America may be obtained on request at the office of the Executive Secretary of the American Academy of Allergy.

Individual surveys have been reported from many parts of the United

States and other countries. Hyde[80] reported his observations on grass pollen in Great Britian. The chief pollen bearing grasses are confined to the lowlands, those within altitudes below 1,250 feet. Atmospheric pollution of pollen grasses are greatest in neighborhood of the lowlands and falls off rapidly with distance therefrom. In Great Britain, the pollen season begins at the end of May and continues to mid-July east and north. In the lowland of Scotland, pollenation occurs from one to seven weeks later. Pollen release was noted mainly in early morning and later afternoon. The highest concentrations were those noted close to grass fields. Hyde noted that the main index of grass pollen varies from station to station, from season to season, but not as much as from place to place. High counts vary from station to station daily. Two hundred and twenty species of grasses are found in England. About twelve are important as causes of hay fever. Sweet vernal, meadow foxtail, perennial rye grass, and fescue, are most important.

Fly[51] reports his aerobiological data for Miami, Florida, covering a two year period (March, 1947 to March, 1949). The report is a compilation of pollenating periods of representative flora; chronology of pollenating periods and summaries of meteorological data. Using standard techniques, approved by the pollen committee of the American Academy of Allergy, studies were carried out. In conjunction with Caribbean pine pollen, she felt that wind velocity and direction had little bearing on maintenance of an air load of a known Anemophilous pollen. The only factor which was demonstrated to have a bearing on lowering the pollen air load was direct precipitation of rain. She suggests a method for studying radial dispersion of pollen. Ambrosia elatior (short ragweed) grows to a height of six feet in Florida. Only 20 grains were counted on exposed slides during a seven-month study and very few clinical cases were observed.

Palay's[120] survey of Miami Beach covers pollen from 1948 to 1949. He reports grass pollen is insignificant, ragweed pollen negligible during September and October. Australian pine has a definite pollenating season with large amounts of pollen from January to February.

McDonald[108] has an excellent discussion of pollen in Florida, and states that ragweed was present in the area of Jacksonville for five days with a high count of 16, and Miami for two days with a count of 9. Twenty-eight varieties of trees pollenate from January to March. Pine pollenates from January to February.

Klotz and Bernstein's[99] survey of pollens that are important in Florida is excellent. The pollens of the following grasses were noted: Bermuda, Johnson, timothy, St. Augustine, Natal, and rye. Pasturage grasses are also important. The following trees are important: pecan, ash, adler, and Australian pine (Southern Florida). The weeds which are pollen producers are giant and short ragweed, English plantain, spring amaranth, redwood, pigweed, Jerusalem oat, sheep sorrel, yellow dock, and water hemp.

In the northern part of Florida, the pollens are usually those found in the southeastern part of the United States which means less molds, more ragweed and more tree pollens, especially pecan. In the middle of Florida, less molds, more grass, plus ragweeds, oak and Australian pine are found. In southern Florida there is no ragweed but there are grasses, Australian pine, and molds.

Mulligan[116] reports on a ragweed elimination campaign in Reading, Pa.

In Chicago we have not felt that a ragweed elimination program is worth the cost involved.

Rowe[140] presents an extensive review of the airborne allergens in Northern California. He feels that mold allergy in this region is of minor importance to pollen allergy.

Perlman[123] notes that common ragweed has finally invaded the Pacific Northwest which has in the past been free from these hay fever producing plants. The pollen counts have been minimal and no clinical hay fever due to ragweed has been reported. The local pollen season may extend from February to November due to the mild weather. He believes that control and eradication methods would be inexpensive and relatively easy.

Jones[84] studied the time of day of pollen shedding of some hay fever plants. He found giant ragweed measured 20. ± 0.2 microns, shed its pollen from 7 a.m. to 1 p.m. during August, September, and October. Timothy pollen granules measured 36.6 ± 0.9 microns pollenating from 4 a.m. to 9 a.m. in June and July. Using petroleum jelly coated slides, the number of pollen grains caught during thirty-minute intervals per 16 sq mm area was used as a measure of the amount of pollen shed. Between 90-99 per cent of the pollen shed was liberated by most species within three to four hours each day. Temperature of less than 60° F. inhibited shedding in some species. Wind movement was important in speeding up anthesis, dehiscence, and dispersal. High relative humidity delayed pollen shedding but did not inhibit it.

Larsen[93] reports his observations regarding climate in relation to allergies in Hawaii. He noted that ninety-six different pollens were possible allergens. Sugar cane showed a high concentration of pollens there during the months of November, December, and January.

Trees did not pollenate heavily and were unimportant. Hibiscus becomes part of dust problem due to large amounts of heavy pollen. Many have large reactions and specificity of reactions depend on exposure. Algeroba, Amaranth, and Bermuda grass are most commonly present in the air and cause most of the sensitivities. The rainfall varies in different areas from as much as ten inches to as high as 180 inches. The wind velocity is very high. In a study of 10,000 consecutive cases who came to doctors' offices, of the total, 334 came because of allergies, as compared to 1,258 cases of acute upper respiratory diseases. In a study of the plantation population, allergic diseases averaged 1,408 per 100,000 as against 31,549 per 100,000 acute upper respiratory diseases.

Criep and Hammond[28] in their paper on the regional factors in allergy report on the environmental factors affecting allergic disease. The geography, climate, and local air contaminants of Western Pennsylvania, West Virginia, and Ohio all were discussed.

Bieberdorf and Swinny[17] report that the mesquite and acacias, as a whole, are usually considered to be relatively unimportant as hay fever causing plants except in the Southwestern United States. Definite conclusions as to their importance in causing hay fever have not been established, except for the mesquite which warrants consideration in the mesquite growing area. The pollen is not produced in great abundance and is not readily carried by the wind. Acacia pollens have been found to be a cause of hay fever and also a cause of dermatitis, but not by the present authors.

A number of articles appeared in the foreign language literature in regard to pollen. Wildfuhr[192] studied the importance of weather, factors in reaction to allergy tests, and desensitization. Pinto[126] reports on allergy in Santos, and Sabatelli[141] on allergy caused by Ambrosia in Italy. Solari[160]

discusses allergy in Argentina, from the standpoint of clinical allergy, foods, molds, and pollen allergens. He says they have relatively few fulltime allergists although they have two allergy societies.

Florentin,[50] *et al*, discusses the atmospheric pollution of the cities, in the Journal, *Concours. Medicine.*

FUNGI

Kaplan[89] reporting on his survey of airborne fungus spores of the Boston area states that Alternaria, Cladosporium, Penicillium, Aspergillus, and Coccosporium occurred as dominant forms. All except Coccosporium showed a fluctuation in seasonal incidence. The peak incidence of total spores occurred during June and in the period from September to November. Absolute humidity greatly influenced the spore count during the spring and fall but not during the summer and winter.

Alvarez and Castro[4] quantitatively studied the airborne fungi of Havana for each of the twenty-four hours during the day, by exposing Petri dishes with appropriate culture media for fifteen minutes in the direction of the prevailing winds. In evaluating their findings, they took into consideration, the number of colonies per dish, temperature, barometric pressure, relative humidity, wind direction and velocity, including cloud coverage. They concluded that the number of colonies or spores deposited on Petri dishes exposed openly increases on a day of increased wind velocity, but this does not mean that the actual number of fungi in a fixed volume of air is greater. The air acts only as the vector but nothing else. Hypersensitive patients are worse on days of west wind, but also become worse when actual quantity of fungi in the air is high, even if there is no wind. In Havana, the quantity of fungi in stationary air is greater at night than during the day.

Targow[168] discusses the interrelation of the variable factors associated with slide counts of Hormodendrum spores. He notes that in making routine Hormodendrum slide counts there are three variables, namely, the number of single spores, the number of individual clumps, and the number of spores within each clump. In the Los Angeles area, the frequency with which each size clump appears is inversely proportional to the size of the clump. The number of clumps encountered annually is almost as great as the number of single spores during most of the years, and exceeds the number of single spores at the peak of the Hormodendrum incidence. Any increase or decrease in one of the variables is paralleled by the other two. The method of counting each clump as a single spore furnishes as reliable an index of Hormodendrum incidence as the method of counting all spores within the clumps, and has the following advantages: (1) saving of time, (2) on theoretical grounds, provides better correlation between the slide counts and plate counts, where both techniques of exposure are used. This method is suggested to be adopted as a standard procedure.

Maunsell[107] studied airborne fungus spores before and after raising dust. The method of trapping spores by sedimentation on open Petri dishes was used. The total number of spores were increased when dust was raised. The increase was from four- to fourteen- fold. Spores received were those of yeast, Penicillium, Cladosporium, and Pullalaria.

Swaebly and Christensen[165] sampled molds in house dust, in furniture stuffing, and in the air within homes, and noted that bacterial counts from fourteen samples of house dust averaged 10,700,000 per gram. Mold colonies isolated from seventy-six samples of house dust collected in

homes in or near St. Paul and Minneapolis in winters of 1950, 1951, and 1952, varied from less than 10,000 per gram to more than 3 million per gram with an average of 179,966 mold colonies per gram. Molds and bacteria were present in some numbers in samples of new furniture stuffing and in considerable number in some used materials. Foam rubber seems to be somewhat susceptible to the invasion by molds, but to a lesser degree. Very few bacteria were found in new or used foam rubber. Molds present in the home may differ, both in kind and numbers, from those outdoors at a given time.

Gregory and Hirst[62] studied the possible rôle of basidiospores as airborne allergens. They used the automatic volumetric spore trap which has a velocity of 10 liters per minute. Vaseline coated slides move past a 2 mm slit at a rate of 2 mm per hour. Sixty per cent of the spores had a diameter of 6.5 microns. In the late summer the spores exceeded pollen concentration; 1000 per cubic meter in twenty-four hours were found. The seasonal flush of Agaries and polyspores need further investigation in conjunction with seasonal asthma.

Lima[97] reported that both perennial rhinitis and bronchial asthma can be caused by sensitization to spores of Ustilago. A patient working in a wheat mill for five years was found sensitive to the Clamydospores of Ustilage tritici. Good results were obtained by specific therapy.

Furness and Maitland's[55] most provocative study on certain dusts reveals that both bacteria and fungi in large amounts were found in cotton linters. Among the bacteria gram negative bacilli, of the genus Bacterium, were present and among the molds, Aspergillus Niger and Penicillium Sp. were noted.

In a continuation of the above study, Clayton and Furness and Maitland[23] prepared extracts by seven different methods from four sources. Reactions from these solutions among cotton workers gave rise to immediate or delayed reactions. Ninety per cent of those tested gave delayed reactions, while 30 to 40 per cent gave immediate reactions. Reaction does not indicate hypersensitivity to Bysenosis, but does indicate something in cotton dust causing hypersensitivity.

The members of International Correspondence Society of Allergy were asked what molds are used in routine testing. Of all the replies, nearly all included the following: Alternaria, Aspergillus, Hormodendrum, Penicillium, Helminthosporium, Mucor, Monilia, Cephalothecium, Rhizopus, Smuts, Fusarium, and Pullalaria.

Several other articles are of interest. Ghillini[57] discusses fungus spores causing allergic sporosis, and Griffith[63] studied antibiosis between wind borne molds and insect larvae with wind borne eggs.

DIAGNOSIS

Schiller and Lowell[145] described in the inhalation tests as a diagnostic procedure with special emphasis on the house dust allergen. Seventy-five patients were studied from the standpoint of history, skin reaction, and inhalatation tests with pollen extracts of birch, oak, timothy, ragweed, and extracts of Alternaria, Hormodendrum, and house dust. Patients were divided into groups because of the way they reacted to inhalation tests to house dust, other allergens, or patients in whom attacks could not be induced by inhalation of the allergens.

Herxheimer and Prior[73] report on their further observations of induced asthma and bronchial hyposensitization. From their studies they conclude

that only a small fraction of chronic asthmatic patients will benefit from this method. The method involved the inhalation of allergic aerosol from a closed spirometer circuit, described by Herxheimer in 1949, in which the inhalation time is measured. This method can be used for diagnosis as well as for specific bronchial hyposensitization.

Feinberg, Stier, and Grater[45] suggest a quantitative evaluation of the degree of sensitivity of patients with ragweed pollens. These investigations use the response of the eye, nose, and bronchi to a specific antigen. Twenty patients with ragweed pollenosis without desensitization therapy showed greater sensitivity than that found in another group of twenty ragweed sensitive patients who had had more than one year of such treatment. There was a correlation between the history of clinical symptoms in a particular shock organ and the degree of sensitivity, as shown by quantitative tests, in various tissues.

The question is frequently asked: "Is it safe to test and treat by specific hyposensitization during pregnancy?"[189] An inquiry among the members of the International Correspondence Society of Allergists revealed that the answers were in the affirmative, utilizing small doses and testing by the scratch test. Our own experience is similar to the above.

Friedewald's[53] investigation as to whether or not skin testing allergic patients is worth the effort reveals the following: 131,865 skin tests were performed on 1900 patients. The most common reactions in order of their frequency were: chocolate, milk, wheat, tomato, malt, corn, orange, black pepper, and coffee. Russian thistle, Bermuda grass, house dust, tobacco, chicken feathers, ragweed, and cow's hair led the list of inhalant reactions in West Texas. He suggests that food testing is time consuming, expensive, and relatively unimportant, but of some importance in urticaria, hay fever, asthma, childhood and adult eczema. He believes skin testing is a safe procedure if proper precautions are observed. We believe skin testing is worth the effort and often serves as a short cut to the finding of the offending agent.

Swain and Becker[166] quantitatively studied by skin testing the whealing reaction of histamine and ragweed pollen extract. Variations in the site response to constant doses of intradermally injected histamine were observed. They conclude that the antigen-antibody portion of the wheal mechanism is not implicated in the site differences, but rather, it must be inherent in the differences of the skin itself. Within the range studied, the dose response of histamine approaches lineally in both logarithmatic and semilogarithmic plots. The variation in histamine dose-response data is sufficient to account for the variation encountered in ragweed dose-response data. Within the limits of the technique employed, there is no evidence that there are other active substances besides histamine mediating the cutaneous whealing reaction induced by a specific antigen.

Morrison[114] describes a new instrument which is a precision microscratcher. The difficulty in using this scarifier is that it requires depth setting for each individual skin. The scratches persist for a week or longer, the method is too slow, is too complicated mechanically, and too expensive.

Lovell, Warren, *et al*[99] report a most interesting group of reactions precipitated by a "Hay Party." The overwhelming exposure of a group of students to old hay produced a large number of symptoms in individuals who had had previous allergic reactions and some developed symptoms for the first time. Of forty people attending the party, twenty-four had allergic symptoms. Sixteen had symptoms that evening. Twenty-four had

hay fever symptoms and of these twelve had asthma symptoms. Exposed Petri dishes with Sabaraud's media revealed Alternaria, Hormodendrum, Aspergillus, Penicillium, Rhizopus, and yeasts.

A question frequently asked by patients is "how do you tell when you have been cured(?)", in relation to hay fever. Most answers received from a number of the letters of International Correspondence Society of Allergy[191] state that after two consecutive years without symptoms following treatment and with negative scratch tests, approximately 85 per cent will be all right for three years. In our experience after three to five years of specific therapy with good results, the probability of recurrence in the next two years is slight. Thereafter proper and adequate exposure will give a recurrence in a large number. However, we have had some sustained "cures."

Hay fever "X" of the south still remains of unknown etiology, although many factors are known. Bowen[18] says in the years of 1950 to 1951, patients had universal symptoms, with 1952 being maximal.

Derbes[31] says that hay fever "X," or otherwise known as summer hay fever of unknown origin, has been suspected by one of his colleagues to be due to an allergen which is a drop released by plants and grasses. In this article, there is a long discussion on "guttation" over "transpiration." This condition is still a question mark.

Harley[70] reports an interesting group of cases with symptoms of rhinorrhea and sneezing. In one case, skin tests were negative to tree and grass pollen but were positive to the juice of grass leaf and bark of beech saplings. In a second case, symptoms developed when pulling new potatoes, and in another, symptoms of allergy developed when injected with adrenalin.

Waldbott and Merkle[179] present clinical evidence implicating pollen as being a causative agent for urticaria. In these cases, seasonal onset, periodic recurrences, positive skin reactions, and reproduction of hives by insufflation of powdered pollen in the nose were characteristic. These cases respond to specific hyposensitization and there were concomitant allergic syndromes such as hay fever and asthma. We have seen several cases of the above. The response to therapy has been excellent.

Swinney[167] reported in an article dealing with pollen and nasal allergy in the southwest, and calls attention to the longer growing season with smaller daily pollen counts than elsewhere. Seasonal patients with single allergies are exceptional, and cases of multiple and perennial sensitivities are of high incidence. His impression is that patients in the southwest are, in general, less sensitive than elsewhere and, therefore, require heavier concentration of extracts for diagnosis and larger doses for treatment. He says that small dosage therapy is a failure in the southwest.

Diamond[33] reports a patient with perennial allergic symptoms under specific hyposensitization with ragweed, timothy, plantain, and house dust, over a period of seven years, experienced painful inflammation of the conjunctiva on those occasions, twenty-four hours after each treatment. The reaction disappeared when dosage was reduced about 50 per cent, and cleared up with the use of antihistamines.

Miller,[112] in a very interesting and descriptive article, calls attention to the development of difficulty in hearing associated with allergic rhinitis. We have frequently found this to be the case in seasonal and perennial allergic rhinitis.

Gordello[61] calls attention to the fact that in a statistical study of allergic

children, he found 71.8 per cent to have significantly positive skin reactions. The most important positives were obtained with house dust, pollen, fungi, and inhalants extracts. This is essentially what we all ascribe to.

Dutton[37] calls attention to the fact that airborne soil bacteria may be important in perennial hay fever. Other important articles, which are related to ragweed, are those of Tuft and Heck[173] on the importance of seasonal inhalant allergies, in atopic dermatitis, and Fisher's[48] immunologic phenomenon in relation to ragweed dermatitis.

NON-SPECIFIC THERAPY

Many substances have been brought forth for the non-specific control of symptoms associated with pollenosis. In our experience, each drug has to be tailored to each patient's needs. None have yet equalled the bronchodilator effect of epinephrine or the vasoconstrictor effect of ephedrine. The number of drug combinations which are added each year make the pharmacopeia of drugs used for pollinosis and allergic rhinitis a formidable one.

Unger and Unger[175] report the prolonged action of a suspension of epinephrine and a glycerine base. Such a compound is Susphrine. In this compound, however, the actual concentration of the base is also increased.

Mosko and Snider[159] report their observation with Visammin (Khellin). Giving doses of 120 mg daily to patients with chronic asthma, the bronchodilator effect was evaluated by comparison with known bronchodilator drugs using clinical and laboratory methods. No significant bronchodilator effect of Visammin given orally or intramuscularly could be demonstrated.

Ogden and Cullich[119] report that Orthoxine is a useful bronchodilator drug in doses of 100 m to 200 mg.

Eisenstadt[43] studied the effect of a new drug combination useful as a bronchodilator. The single dose dual combination tablet is known as Nephenalin, and combines sublingual and oral administration. The thin outer coating contains 10 mg of N. isopropyl arterenol hydrochloride. The inner core contains an antiasthmatic combination of ⅜ Ephedrine HCL, 2 gr of Theophyllin and ⅛ gr of Phenobarbital. Mild to excellent results were noted in fifty-one out of sixty-two patients. We have found this drug not very effective. In mild cases it has been of some help. The authors note mild transient side effects consisting of palpitation, nervousness, tremors, and excessive perspiration in about 26 per cent of the patients.

Widman and Keye[188] report their studies with a tablet containing 200 mg of Tyrosine, 2.5 mg Pyridoxine HC, and 10 mg Niacinamide. The authors have previously demonstrated the vasoconstrictive properties of the amino acid tyrosine, one of the epinephrine formers, when administered orally, together with the precursor of its decarboxylating coenzyme combinations in conjunction with Niacinamide, and suggest it would be helpful in allergies. Their compound not only possesses antihistaminic properties but also through its rôle in the dehydrozenase, coenzyme I, probably aids in conversion of the tyrosine into epinephrine, or a clearly allied substance. Their results with hay fever, histamine headache, urticaria, and penicillin reaction are promising. Note: Our own results have been disappointing with this compound.

The authors feel that certain additional findings may be part of the allergic symptom complex, namely, tendency to hypotension, flat sugar

curve, low basal metabolic rate; epinephrine is a specific counterirritant of the above derangement. An attempt to flood the organism with natural precursors of epinephrine is an attempt to increase the available stores of this substance.

Trethewi[171] reports the effect of Para-aminosalicylic acid in the allergic person. He feels that PAS inhibits release of H. substances.

Krohn, Pottenger[91] in their studies on allergic rhinitis report the use of Tocopherol therapy in conjunction with a diet of high protein, low CHO, lecithin, B_6 complex, raw liver, and salt. Adult diet contained 4500 calories, and the children's diet contained 2500 calories, plus 20 to 25 mg of D.L., Alpha, tocopherol acetate. Results were excellent and relieved symptoms in those who could not be helped previously.

Jonez[86,87] reports in a special article, the uses of histamine. He says that he has found repository histamine injections to have nearly the same therapeutic effect in allergy that cortisone and ACTH have. He has also used it in hay fever. Histamine diphosphate suspension contains 2.75 mg/cc in menstruum of oxycholesterol derivatives, dissolved in peanut oil. This product is marketed by Endo under the trade name of Histapan. Johnson, Sheldon, *et al*[82] report their studies on the use of a Phenacetin-caffeine (PC) combination in the treatment of hay fever. In a group of six unselected ragweed hay fever patients using four combinations, including placebo, antihistamines, an antihistamine PC combination, and a PC combination, they report results at the end of a trial period of four days with each material. No essential differences were noted between those who received placebo and PC. There was very little difference in the effectiveness of the antihistamine alone as compared to its combination with Phenacetin and caffeine.

Bernath[15] says lobeline has no specific therapeutic effect in allergic rhinitis.

Hillis[74] reports his studies on assessment of cough-suppressing drugs. He found that morphine, diamorphine, and Amidone were proven potent suppressants, and that Codeine was not superior to those mentioned.

Allergex[6] as a control for dust sensitivity is reported as an excellent adjunct but not as a substitute in the treatment of dust sensitivity.

Lovell, Mathews, *et al*[100] suggested the use of G4 (5 chloro- 2 Hydroxyphenylmethane) as a means of control of fungous growth.

SPECIFIC TREATMENT

An editorial[40] in ANNALS OF ALLERGY calls attention to the fact that for the present, there is no single drug or procedure which can do more than allay certain minor phases of the allergic symptomatology except that directed to the offending allergen.

Another editorial[41] on "The Editor's Page," "The Treatment of Hay Fever," discusses the problems involved. Although nihilistic in tenor, we urge everyone to read this excellent short essay. Certainly it must be provocative of some good to come although amusingly cynical, it certainly should set those of us interested in the furthering of allergy to lots of introspective thought and it is hoped, deeds of import.

Very little has been added to the specific treatment of pollenosis. This is to be expected since the specific and pure antigen or antigens responsible for the symptoms have not been identified.

Loveless[101] reports her studies on a group of 101 ragweed-sensitive subjects who had been treated from two to thirteen years. These patients had

received in the past years anywhere from eight to forty injections. With an aqueous oil emulsion depot injection containing Falba and mineral oil, Loveless was able to obtain good results using anywhere from four to seven injections. She was able to improve her results from 63 per cent to 75 per cent and cut the constitutional reaction from 50/100 aqueous to 15/100 injections using the aqueous oil emulsion as against the aqueous extract.

Sternberg[163] studied a group of summer hay fever patients who were uncontrolled when treated with pure timothy extract. Thirty-six of fifty patients reported better results when treated with a mixture of grasses. Thirty-two cases who were not highly sensitive and who had reached their maintenance dose, were changed from timothy to a mixture of grasses, thirteen developed constitutional symptoms when given the same quantity of mixed grass pollen.

Nine patients gave more marked skin reactions to some of the other individual grasses than to timothy with the same strength extract. This gives evidence that grass mixtures contain specific antigenic factors which are absent in pure timothy extract. Sternberg recommended that patients not doing well on pure timothy pollen extract should receive mixtures of common grasses or an extract of mixed grasses should be used routinely.

Small and Small[157] present a system of constant percentage increment of antigen dosage for desensitization which they feel will facilitate both the treatment of allergic diseases and the recording of the patient's progress. However, we fail to see any particular advantage occurring from the use of what appears to us to be a somewhat cumbersome system.

Silbert[153] describes his experiences in treating 121 patients with perennial or seasonal rhinitis combining injections of Chlor-Trimeton and allergenic extracts. He felt he required fewer treatments than those treated in the conventional manner. The final dosage achieved was considerably higher with this method and constitutional as well as large local reactions were markedly reduced. Silbert felt that this method appeared to increase the number of successfully managed cases.

Levin[96] discusses the optimum dose of pollen in the treatment of pollenosis in children. He starts his pre-seasonal therapy with a solution of 1:10,000. Usually the dose is .05cc and is increased weekly until a top dose of .50cc to 1.0cc of 1:33 solution is given. Twenty-five injections are usually needed. The maximum dose is judged by the size of the local reaction. During the season the dose is cut in half and between seasons the maintenance dose is half the maximum dose. This is given at intervals of three weeks. Six to eight weeks prior to the season, injections are given weekly to the top dose. Co-seasonal injections are given in doses of .01cc to 0.1cc intradermally of the weakest solution that shows a positive reaction, at three-day intervals (1:10,000 dilution). The routine use of epinephrine is not advised.

Van Dishoeck[177] asks the question as to why the symptoms of hay fever decrease after specific desensitization. After specific desensitization the reagins do not diminish and the allergens are not destroyed. In desensitization, with large doses of antigens, antireagins came into existence which block the reagins and inhibit the reactions between allergen and reagin.

An excellent discussion of the treatment of hay fever in children is noted in Ratner's[135] article. Other articles can be found in the foreign languages and each discusses the problem of local importance.

Reactions following therapy to both specific and non-specific substances are of such serious import that we feel they should be mentioned.

Arsenic has been reported as the causation of toxic reactions many times but is being mentioned again only to call attention to the danger of its indiscriminate usage. Silver[154] and Wainman report chronic arsenical poisoning following the use of "an asthma remedy." Two cases were reported in which clinical symptoms of keratosis, gastroenteritis, hepatitis, and mild neuritis were noted.

Pascher and Wolf[121] report cutaneous sequelae following the use of Fowler's solution in conjunction with therapy for asthma. In two cases manifestations of arsenicalism are described with the development of keratosis, keratoderma, and arsenical pigmentation.

Ufford[174] calls attention to sudden death during prolonged therapy with ACTH. The patient was being given an intravenous drip of 1000 cc of 5 per cent glucose in water with 25 mgs of ACTH over a period of twelve hours. During the ninth week and the sixth time, after onset of the drip, the patient suddenly died. At the autopsy, no significant pathology was noted.

Hellman[72] reports an allergic reaction to procaine amide in a fifty-three year-old man who was given 1.5 gm of procaine amide orally followed by 250 gm every four hours. After the third dose, he developed a maculopapular erythematous rash, severe itching, nasal congestion, slight generalized adenopathy, and a fever of 102° F. Cessation of procaine therapy and institution of Benadryl caused a complete relief of symptoms in twenty-four hours. At a later date, oral testing caused a similar reaction which responded to Benadryl.

Walton and Elliot[183] report on a patient who previously responded to intravenous ACTH and was given daily increasing doses of Pyromen by the intravenous route. After the seventh dose (0.5cc) the patient began to develop increasing dyspnea, not controlled by epinephrine, became cyanotic, and respirations became markedly depressed, and he died eighty-five minutes after the injection. Autopsy showed a striking example of intense bronchial and bronchiolar obstruction due to mucous plugs and mucosal edema; death was due to asphyxia.

Fenton[46] reports a case history of a hay fever patient who had severe leg pains in correlation with specific hyposensitization of ragweed pollen in the fifth year of therapy.

Fatal allergic reactions to penicillin are occurring far too frequently not to be a constant source of concern. In an editorial in the *Journal of Allergy*,[39] caution is advised in those allergic patients who have previously shown reactions or sensitivity to penicillin. Skin testing is suggested as a possible aid to foreseeing and avoiding reactions; either the scratch or intracutaneous test is advised. We feel that the individual who shows evidence of increasing severity of reactions with each succeeding contact with penicillin is a candidate for a probable anaphylactoid reaction.

ANTIHISTAMINES

An excellent review by Haag[61] covered the pharmacologic and therapeutic aspects, as well as the side reactions, of the antihistamines in a general survey. A similar critical review and general discussion on the subject of histamine antagonists was presented by Noelpp-Eschenhagen.[117] Mitchell[112A] reviewed the clinical usefulness of these preparations. It was his opinion that except for their value in relieving uncomplicated hay fever, urticaria and bronchial asthma in infants, they have been a

great disappointment. He further felt that their indiscriminate use by factory employes and motorists has resulted in new industrial and highway hazards because of their toxic side reactions. Loew[98] discussed in general, the pharmacological properties of the antihistamines in relation to allergic and non-allergic diseases.

Maietta[104] reported on a study using a single injection treatment for hay fever, combining the simultaneous administration of a large dose of pollen antigen and an antihistaminic. Although no proctocols were included in this report, it was the author's finding that of fifty pollen-sensitive patients receiving this prophylactic treatment (seven to fourteen days prior to the onset of the season), nineteen had excellent results; twenty-three good; six fair; and two poor. Aside from consideration of the other aspects of this paper, it has always been somewhat difficult for us to categorically classify degrees of sensitivity by skin testing.

Thomas and Kelly[169] found that the Elixir of Ambodryl was palatable and well tolerated, controlling symptoms in about 75 per cent of those patients in which it was used and without significant side reactions. McGavack,[110] *et al,* conducted a study on the long continued use of this antihistamine. Forty-five of their patients had received 75 to 300 mg of Ambodryl for periods of time ranging from twelve to thirty-one months. Drowsiness was the only side effect observed, appearing early in the treatment in four subjects, but did not necessitate discontinuance of the drug. They conclude that Ambodryl is a highly effective, relatively non-toxic antihistamine which may be employed for prolonged periods of time without losing its effectiveness. This finding of continued effectiveness over long periods of time would seem to be at variance with previously available data on the prolonged use of antihistamines.

Mothersill[115] felt that the combination Co-pyronil resulted in prolonged antihistamine action.

Of 102 patients suffering from hay fever, ninety-four (92 per cent), according to Silbert,[152] were benefited by Phenergan therapy. He treated a total of 216 patients with various allergic complaints, with this preparation and only 12 per cent experienced side effects, the most important being drowsiness. Unfortunately, no mention was made as to whether or not concomitant hyposensitization therapy was administered to these patients.

Spearman[161] used intravenous Decapyrn as supplemental therapy in 100 cases of allergic rhinitis, eighteen being of the seasonal variety. He felt that such a regime increased the immediate relief obtained by the patient and gave results superior to those obtained prior to its use. Side effects were surprisingly mild.

Shure[151] *et al* studied a combination of three antihistamines, each in a dose approximately one-third the average dose, by clinical trial and quantitative bio-assay. Good relief was obtained in over 70 per cent of the patients with allergic rhinitis. This is compared with approximately 15 per cent when placebo was used. The incidence of side effects was minimal. Histamine induced wheals were inhibited by the combination of antihistamines in a dilution greater than that of any single component of the mixture and the authors suggest a synergistic action.

Wittich[194] found Dibistine to be as effective as other various antihistamines without, as a rule, as many unfavorable reactions. In his series, sixty-seven patients suffered from seasonal hay fever of trees, grasses, or weed etiology. The combination of the two antihistamines, proved more effective with less side reaction than when each was used singly in

the full regular dose. There apparently appears to be a better balanced summation effect of the two than that effected by the use of a single one. It has been our experience with this preparation that the combination of Antistine and Pyribenzamine approximated the efficacy of Pyribenzamine alone in full dosage but with considerably less side effects.

Simon and Toohey[155] treated fifty patients with seasonal and perennial rhinitis, urticaria, and angioneurotic edema with Dibistine four times daily and felt that 92 per cent were improved, with undesirable side effects occurring in only 6 per cent. Several patients who experienced drowsiness after taking 50 mgm of Pyribenzamine alone had no significant complaints after taking two Dibistine tablets. They concluded that the combination of Antistine and Pyribenzamine gave good therapeutic results with a minimum of undesirable side effects; and offered as explanation of the excellent results of combined smaller dosages as being due to synergistic action. They further attempt to explain the basis of less side effects on mutual antagonism, which would appear to us to be untenable and certainly more readily explainable on the basis of smaller dosage.

Schoenkerman and Justice[147] treated fifty-eight patients with a combination of an antihistaminic and a flavanoid (Rutin). They felt that 75 per cent of the patients received greater relief from this combination than with the antihistamine alone. The season in which this clinical evaluation was undertaken was a mild one as reported by the authors.

In a study of Foralamine Fumarate by the investigators of the therapy committee of the American Academy of Allergy,[7] the general concensus of opinion was that it is "just another antihistamine drug." Of eighty-six patients with seasonal allergic rhinitis, eighteen were slightly improved and thirty-seven satisfactorily improved. Side effects were those usually encountered with antihistaminics. Our own experience with this drug belies it being "just another antihistamine." It was our experience that its effectiveness did not even approach the weakest previously available histamine antagonists; however, there were very few side effects.

Trimeton and Chlor-Trimeton solutions were used locally on the nasal mucous membranes of 144 patients with allergic rhinitis by Schaffer and Seidmon.[144] Their observations revealed that nasal instillation of these antihistamines was safe and that they provided sustained vasoconstriction of the mucosa without "rebound" phenomenon. They further were of the opinion that this form of therapy was an effective method of palliation, not intended to substitute for accepted allergic diagnostic and therapeutic procedures.

Hurwitz[79] reported 83 per cent effectiveness in the use of Trimeton Opthalmic solution in ocular allergies. The parenteral form of Chlor-Trimeton was used by Bernstein and Klotz[16] in 326 patients representing a variety of allergic syndromes including hay fever. It was their feeling that this was a potent antihistamine, therapeutically most effective in hay fever, vasomotor rhinitis, urticaria, and angioneurotic edema. It was their feeling that it opens a wide range of clinical usefulness where more rapid antihistamine effects are desired or the condition of the patient precludes oral administration. The side effects experienced were relatively small.

Using serial dilutions of ragweed extract, Endo Dust, and Histamine intradermally, Fond[51A] found that Perazil caused no reduction in skin reactivity one hour after its administration but was most effective after six to twelve hours. Chlor-Trimeton was most effective from one to two hours, and its effect lasted as long as four hours. Pyribenzamine and Benadryl

showed their greatest effect one hour after administration with their action waning within two or three hours. It was his opinion that the drug of choice to be used in dermographism apparently was Perazil in a dose of 100 mgm, given the preceding night, permitting a more accurate appraisal of skin reactivity in allergic individuals.

Cronk and Marty[29] presented some data that might suggest that a significant percentage of "colds" are allergic reactions which respond favorably to antihistaminic therapy.

ADRENOCORTICOTROPIC HORMONE AND CORTISONE

The year 1952 witnessed a general trend in the use of these hormones, with therapeutic uses outweighing fundamental mode of action studies. The benefits, as well as most of the side effects were well known by this time, and, as a consequence, usage and effect of therapy on allergic diseases seemed to fill the literature.

Brown[19] presented an excellent review on the subject, covering some of the highlights about ACTH and its implications in ANNALS OF ALLERGY, stating "that it has not, in any sense of the word, helped us discover the cause of allergic disease." A summary[137] of the conference on the effects of cortisone in general medical problems was also presented. A report by Pickering[125] gave an outline of the effectiveness of both ACTH and cortisone. The rôle of both these hormones in allergic disease, with a summary of the basic understanding of the two, as originally presented by one of us (A.L.A.)[1], was seen in the Brazilian literature.

Anderson[8] further observed that neither ACTH or cortisone produced any change in the intradermal reactions of the allergic patient, or any change in the sensitivity to histamine. Hayes and Dougherty[71] noted the effect of ACTH and cortisone on antibody synthesis and upon the rate of disappearance of the antigen as studied in mice which received single intravenous injections of horse serum. The greater the amount of antigen, the more hormone was required to suppress the formation of antibodies. Their work seemed to indicate that antigen persisted in the tissues in the period of inhibition of antibody synthesis.

Appel, Fulton, and Orr[10] presented observations on essentially normal young combat veterans treated with ACTH and cortisone for frostbite injuries. In order of frequency, they reported the following side effects: mooning, impaired glucose tolerance curves, hypertension, acne, hirsutism, edema, and psychic changes.

Allergic reactions to cortisone and corticotrophin were reported by DeSeze *et al.*[32] These authors gave details of six patients demonstrating allergic reactions or idiosyncrasy to either of these hormones; in one patient, causing reappearance of hives which had been previously relieved by an antihistaminic drug; in another patient, showing lack of benefit from either ACTH or cortisone in an anaphylactic alimentary reaction. The author attempts to offer an explanation for this strange behavior.

Edward[42] presents the effect of the two hormones in the treatment of hay fever. This author concludes that the drugs are useful, but not curative, especially in hay fever asthma.

Irons[81] feels that these two hormones should be used only on the acutely ill patient, not in mild conditions. Hollender[77] reported on psychological reactions to cortisone in a patient who suffered both from a psychological illness and a long-standing ocular disturbance for which she had received good psychotherapy. The author feels that the reactions to cortisone was

determined by the personality makeup of the patient as well as the pharmacological action of the drug, and suggests that cortisone addiction might become a serious problem in emotionally disturbed patients.

Hampton[67] presented a good general discussion on the use of ACTH and cortisone, the advantage of intravenous as intravenous-intramuscular combined therapy. He also comments on the side-effects of the drugs and notes that the effect is usually only temporary.

The effects of the hormones on patients suffering from multiple sclerosis were reported by Glaser and Merritt.[59] One-third of their thirty-three patients showed significant improvement on therapy, but reappearance of active clinical symptoms occurred when the drugs were withdrawn, or when a placebo was substituted. The effects of the hyperadrenal state induced by ACTH and cortisone were studied in fifty-eight patients with disorders of the nervous system. Deleterious effects included weight gain, water retention, hypertension, hyperglycemia, mooning, hirsutism, acne, and generalized asthenia. No significant alterations were noted by these authors in patients with progressive muscular dystrophy, myotonic atrophica, Parkinsonism, Wilson's disease, and Sydenham's chorea.

The use of cortisone nose drops was discussed by Glaser,[58] noting that 5 per cent solutions were without much benefit. He suggests that stronger solutions might be beneficial. McCombs[109] discusses serial courses of corticotrophin or cortisone in chronic bronchial asthma. The author showed the costliness of such therapy and notes that ACTH-gelatin solutions, long-acting, gave the best results at the lowest cost.

Prickman et al[128] discuss the antihistamines, cortisone, and ACTH in respiratory allergy, and find the former to be effective in 60 per cent-70 per cent of the patients, while ACTH and cortisone were most effective in asthma due to pollens, and they recommend oral cortisone for relief of hay fever symptoms alone. Rappaport and his co-workers[132,133] studied nasal biopsy tissues of ragweed patients as compared to nonsensitive individuals. Of forty-five patients studied, thirty-two received ACTH or cortisone, and six were normal. They noted a decrease in the intensity of the staining of the ground substance in addition to other changes in the stained specimens studied, all of which could be reversed by administration of cortisone. The authors believe the changes seem to be caused by increased depolymerization of the mucoproteins in the ground substance.

The psychological response to ACTH, cortisone, hydrocortisone, and related steroid substances was reported by Rome and Braceland.[138] The authors analyzed results seen in twenty-six patients suffering varying mental and physical disorders. Euphoria occurred in 60 per cent of the patients; anxiety in 25-30 per cent. Lidz reported the appearance of psychoses in three cases where these hormones were used.

Schwartz *et al.*[149] studied twenty-five selected hay fever patients who had received oral cortisone, 100 mg per day in divided doses, for fifteen days, and who were also given a low salt diet and fifteen drops of saturated potassium iodide drops three times daily. They noted that twenty-one of twenty-five patients studied had marked to complete relief, one only moderate relief, and three had no relief. Side effects of a mild, brief nature occurred in nine patients. These authors suggest that combined ragweed hyposensitization with oral cortisone therapy produced greater relief than any other method of treatment. Stier and his co-workers[164] studied forteen patients with hay fever or hay fever and asthma due to ragweed pollen. These patients received oral cortisone for a short time

several months before the ragweed season and again during the pollenating season. Quantitative changes in the mucosa of the eye, nose, and bronchi were determined as to sensitivity. Symptoms of hay fever were more difficult to control than those of asthma. Ten patients developed untoward reactions and cortisone had to be discontinued in three patients because of severe complications. The authors conclude that cortisone given out of season decreased sensitivity of the mucosa to ragweed extract. After relief from cortisone during the pollenation season, a weaker dilution than previously used, prior to the season, produced a reaction on the mucosa. The time of disappearance of intradermally injected saline or histamine was somewhat lengthened by cortisone, and the disappearance of Hyaluronidase was markedly prolonged. They also noted no detactable change in the titers of the skin sensitizing antibody or the thermostable antibody in patients treated with cortisone.

Psychotic reactions associated with ACTH and cortisone were also noted by Tourney and Gottlieb.[170] They noted that minor mood disturbances (euphoria or depression) were reversible when treatment was discontinued. In addition, the patient may demonstrate transient effects, such as: increased tension, irritability, fearfulness, and insomnia. However, psychological changes may be greater in degree and cause much concern. The authors present four illustrative case reports. They stress the importance of the physician's alertness to the psychological and toxic manifestations of these hormones.

Wall and Shure[181] reported on the use of intranasal cortisone suspensions injected in strengths of 2.5 to 5.0 mg. per cc, in doses of 0.1 to 0.2 cc into the inferior turbinates of patients with allergic coryza, treatments being given on opposite sides of the nose at three-day intervals. They report that an average of four doses produced lasting improvement from six weeks to ten months in forty-two of fifty-two patients studied. If greater amounts were injected, severe constitutional reactions occurred. They suggest the use of this method in ragweed sensitive patients in late August.

The effect of ACTH, cortisone and histamine[190] on skin testing was reported by survey. Most men feel that skin tests are not affected by the hormones, while there is some questionable reduction with antihistamines. Chevane and Herbay[21] also reported on the use of cortisone in nasal allergy and found good results if used properly. Zussman[196] and Weinman and his collaborators[187] report on the effects of ACTH and cortisone in allergic reactions and also outline the abuses. Grab *et al.*[60] reported on the effect of ACTH in skin, conjunctival, and nasal mucous membrane reactivity to histamine and antigens in man. Dill and Bolstad[34] presented further observations on the local use of cortisone in the nose of patients suffering from allergic rhinitis. Brown[20] continued his excellent survey on the effect of ACTH in ANNALS OF ALLERGY. This was a good, complete, general report. Dragsted[35] presented a fine physiological report on the question of whether specific desensitization affects the adrenals.

Deaths from cortisone in the treatment of bronchial asthma was reported by Jarvinen.[83] One patient, a woman aged fifty-three years, died suddenly after receiving 400 mg of cortisone in divided doses, over a period of four days. The other was a thirty-nine-year-old man, who received an initial course of 550 mg of cortisone, in divided doses, over a six-day span, and then after an interval of five days, the patient died following a second course of cortisone, consisting of only 75 mg. In both patients, postmortem studies revealed bronchial asthma, cor pulmonale,

and acute congestion of the gastrointestinal tract. The author feels that the drug played some rôle in the death of these two patients, perhaps on the basis of vascular insufficiency since regulation of the vascular tonus is closely integrated with function of the adrenal glands. He also stresses that cortisone should be given very cautiously to asthmatic patients with pulmonary emphysema and cor pulmonale.

In general, 1952 showed a tendency to continued use of ACTH and cortisone in selected cases, with constant awareness of the side effects and dangers already known. More emphasis on the psychic effects appeared in the literature than in previous years, giving the physician another major problem to look for. It is the studied opinions of the authors that these hormones are of great value in the treatment of many allergic diseases, if carefully and judiciously administered, but they do not offer replacement therapy for specific avoidance and/or hyposensitization injections. As adjuvants to such treatment they are invaluable.

PSYCHODYNAMICS

It is very interesting to note how much psychodynamics affect certain facets of allergic disease. Where a definite correlation exists between allergen, specific allergen and symptoms, such as, we find, in pollenosis, the psychosomatic findings become minimal.

Abramson's[2] discussion in the *Journal of the American Medical Association* touches on this subject. He calls attention to the trauma which results from a constitutional reaction.

Wittkower,[195] in a paper titled "Psyche and Allergy," relates psychodynamics to the production of hay fever. He noted very few people with hay fever were subjected to analysis. One of the authors has had several patients with hay fever under analysis for other allergies. There was general improvement of the other allergies but the patients still required specific hay fever therapy.

Abramson[2] proposes that therapy of asthmatic patients may be based on their psychologic types. He describes them as anxious, depressed, grieving, hostile, dependent, euphoroid, and phobic. The anxiety type is best treated by sedation; depressed by stimulants including epinephrine; grieving type by increased breathing exercises; sedatives, and sympathomimetic amines should be kept at a minimum. Dependent asthmatics need support, small doses of sedation, and sympathomimetic amines. Euphoroid asthmatics and phobic patients need psychotherapy.

MISCELLANEOUS

Walker[180] calls attention to diagnosis and treatment of rhinitis medicamentosa. The diagnosis is usually established by the history of prolonged nasal medication, constant nasal obstruction, and from shrinkage of nasal mucous membranes. The treatment is complete with drawal of all local nasal therapy, liberal use of analgesics, barbiturates, heat, and occasionally antihistamines. This condition exists more frequently than is usually thought.

Van Alyea and Donnelly[176] discuss the systemic effects of intranasal medication. The medicine is frequently swallowed, leading to many bizarre symptoms. They note that the antibiotic and antihistaminic nasal medication has proven disappointing. They conclude that the nasal solution should resemble physiochemically the consistency of the normal secretion

of the nose, in health: the solution should be isotonic, non-irritating to the ciliary mucosa and the Ph should be slightly acid.

A number of articles which will prove worth reading in conjunction with associated findings in the eye, nose, and eyelids are those of Hanser,[69] Maddox,[103] and Costroviejo.[27]

Fein and Swinny[44] report that not infrequently the only manifestation of seasonal allergy or, as the laity commonly calls it, hay fever, may be eye symptoms. Such a case is reported of allergic irititis which responded to hyposensitization with indicated pollen extracts.

Hunnicutt's article,[78] "The Chronically Congested Nose," calls attention to the fact that this complaint is one of the most common ones seen by Ear, Nose, and Throat specialists. Patients should be taught to avoid excessive nose blowing, and use of nasal vasoconstrictors. He suggests the use of oral administration of propadrine or neosynephrine capsules at bedtime. Avoid fatigue, emotional upsets, chemical, and air borne irritants.

Under this section we will mention articles which we believe are of interest to allergy in general and some phase of pollenosis:

Steinberg and Zimmerman[162] studied stress as it is related to the eczema, asthma, hay fever diathesis. In twenty-seven patients the alarm reaction was studied by the use of epinephrine in an artificially applied stress situation.

Controls and allergic individuals respond normally to epinephrine, using the eosinopenic index as a measure of response.

In patients with allergic, namely atopic dermatitis, abnormal eosinopenic indices were noted, especially "hot room" stress. On this basis, it is felt emotional stimuli can cause acute exacerbation.

An excellent article covering the subject is that of Selye's[150] "Allergy and the General Adaptation." In this article he discusses the precursion of the stress concept, the concept of stress, non-specific stress, and the concept of the general adaptation syndrome.

Ratner and Silverman[134] excellently review the distribution of allergy and the cogent factors in the hereditary concept. Many discrepancies noted in published observations are largely due to different methods of collection of data, the criterion employed in defining the allergic state; and the extent to which inquiry was made. Positive familial history was obtained in about 50 per cent of allergic patients. About 10 per cent of the persons in the random population have major allergies. All individuals are potentially capable of developing allergy.

A number of interesting articles worth perusal are as follows: Watkins,[184] "Allergy in Childhood;" Walton's,[182] "Allergy and Anaphylaxis" Tuft's,[172] "Allergy Problems in General Practice and Their Management" Smyth's,[158] "Allergies in Children," and Pounder's[127] "Life Cycle of Allergic Individuals." A number have been read but not reviewed: Jones,[85] Hunnicutt,[78] Hansen and Fuch,[68] and Alexander.[3]

Peters, Prickman, Koelsche Maytum and Carryer[128] discuss the effects of smoking. Their dictum, "No patient with asthma should smoke" is ascribed to by us. The author feels that smoking tobacco causes bronchitis, bronchospasm, increased secretions, and increases cough.

Macaulay[102] reports hay fever in an individual sensitive to tung nut.

Halpin's[66] most excellent review covered miscellaneous aspects of the field of allergy, generally left uncovered in reviews dealing with the major allergic syndromes.

Fontana's[52] reviews of the recent literature relating to asthma in children

stresses the point that prevention of the allergic state is really the initial phase of therapy. Repeated bouts of dyspnea, associated with sonorous or sibiliant râles, is not uncommon in children leading to upper respiratory allergy. Infection plays an important rôle. Bronchiectasis is often a reversible complication in children.

Gardiner,[56] in a discussion of the relationship of allergy with industry, makes mention of nasal symptoms which may simulate hay fever occuring where there is flour manufacturing, sorting and inspection of grain, manufacturing of linseed oil, lead pencils (Cedar wood dust), paper, paint, seed mills, et cetera. A general survey is presented with suggestions as to the prevention and treatment.

Ragan[130] reports the transaction of the third conference on Connective Tissue. Different techniques are reported by interested workers in the field. Fisher's discussion of hypersensitivity and the hyperadrenal state is excellent. The effects of ACTH and cortisone on immune mechanisms is elaborated upon. Other reports involve technique of studying connective tissue by special staining and the electronic microscope.

Rawlins[136] proposes an hypothesis for the basic mechanism of allergic pathology. Edema is the main pathology in the allergic state. Clinically, this edema is located in the mucopolysaccharide gel of connective tissue. The enzyme hyaluronidase liquefies the gel and thus produces edema. The enzyme is present, in bound form, in or around connective tissue at all times, and is liberated from damaged tissues in large amounts in allergic inflammation of the skin. *In vivo* ACTH or cortisone neutralize hyaluronidase and restricts allergic edema. In the allergic state, an imbalance exists between the building up or breaking down of hyaluronidase and is possibly an autonomic hormonal imbalance in which enough cortisone is not produced to maintain equilibrium. He further suggests that the allergic state is characterized by a condition in which many types of stress produce an imbalance, in the building up and breaking down enzyme system of the amorphous substances of the local shock organ, with localization being brought about through the action of the autonomic nervous system.

REVIEW ON BOOKS

This year we note very few books dealing directly with the problems involved in relation to hay fever and perennial allergic rhinitis. Most of the books deal with data which have a bearing on allergy in general. In our opinion, the books which are of greatest interest are the following:

In *Heredity in Bronchial Asthma*, Michael Schwartz[214] has presented his manuscript in which he correlated the hereditary disposition as a factor in the production of allergic disease. He very carefully brings out the relationship of hay fever and perennial rhinitis to asthma. This excellent monograph is a *must* to everyone interested in allergy.

The Management of Bronchial Asthma, by Herxheimer[209] is an excellent guide to therapy and gives a critical evaluation of all types of treatment.

Paul Kallos[210] has accumulated contributions of numerous men who have devoted a great deal of study to various phases of allergy. This is an excellent treatise and is presented in a book called *Progress in Allergy III*.

The proceedings of the *First International Congress for Allergy*[208] has been published by S. Karger and has been edited by A. S. Grumbach. This excellent book contains all of the important papers that were presented in Basel, Switzerland, in conjunction with the First International Congress for Allergy.

Conn's *Current Therapy of 1952*[201] has as its editor for allergy, Vincent J. Derbes. This section covers the current therapy of fifteen subjects and has such fine reports as "Hay Fever in Children," by Bret Rattner;[201] "Nasal Allergy"[201] by Arbesman; "Bronchial Asthma,"[201] by Unger; "Antihistaminics in Allergy,"[201] by Leo Kriep, and "Asthma in Children,"[201] by Deamer.

Two books on Pharmacology contain a great deal of information of the action of drugs useful in allergy. Salter's textbook on *Pharmacology*[213] deals with the science of pharmacology with special reference to the action of drugs on physiologic mechanisms. It discusses the action, chemistry, and elimination of drugs.

Beckman's *Pharmacology in Clinical Practice*[199] is essentially a text for therapy with a good cross index on drugs.

Symposium on the Influence of the Hypophysis and the Adrenal Cortex on Biologic Relations[217] (Schwabe, Benno and Company, publishers) records the excellent investigation and clinical research of some of the most outstanding men interested in the influence of the hypophysis and the adrenal cortex on biological reactions.

Dorothy Baruch and Miller have written a very interesting book entitled *One Little Boy*[198] which should arouse a great deal of discussion and controversy, especially at the broad applications of psychodynamics in relation to allergy as expressed in the opinion of the authors.

Millman's *Pardon My Sneeze*[211] is a book written along popular lines dealing with allergy. It is an addition to the many books similarly written for the layman.

A number of books have appeared in the foreign literature in our ever-growing library on allergy. Among them are:

Donnatelli, L. and Serafini, A.; *Gli Anhistaminici di Sintesi, Farmacologia e Terapia. Edizionini Scientifiche Italiani Napoli 1952.*[204]

Serafini, Umberto, and Gola, Guiseppe, La Pollinosi, Collano: *Di Attnaltia di Medicina Practica-Diretta da Cesare Frugoni.*[216]

Frouchtman, R.: *Urticaria y Edema Angioneurotico.*[207]

Bariatti, R.: *La Stomaco Nel Quadro dell"Allergia.*[197]

Doerr, R.:[205] *Allergia. Die Anaphylaxie Bd. 2 Immunitatsarektion und Endogene Vergeftering.*

Piantoni, L.:[212] *Bioergia e Allobioergia Prolegoment All"Allergia.*

De Sambucy, A., and De Sambucy, M.:[202] *Asthme.*

Vallerg-Radot,[218] Pasteur, rfi.; *Etudes Cliniques, Experimentales et Theropeutique sur l'Allergie.*

Egon Bruun, president of the Danish Society of Allergological Research and Member of the Executive Committee of the International Association of Allergology (I.A.A.), is editing a new handbook entitled *Who's Who in Allergy.*[220] This directory will be published under the auspices of the Association. This book should help in promoting co-operation among allergists throughout the world. It will contain a list of all existing national allergy associations and their members. The biographical data will contain education, training, qualifications, posts of special responsibility, membership of associations, tenure of official positions of each individual member, professional address, and hours of consultation. The publication will be kept up to date by the issue of addenda where necessary. This handbook is another step in uniting the allergists of the world in furthering their common interests, mutual understanding and to allow for exchange of ideas by recognition of their mutual interests.

Erdtman[206] *Pollen Morphology and Plant Toxonomy (Angiosperms)* has descriptions on external structures of pollen grains of the angiosperms. Theirs is a good section of the preparation of pollen and pollen morphology, and also is an excellent glossary of terms. The book is highly technical but will attract those interested in pollen.

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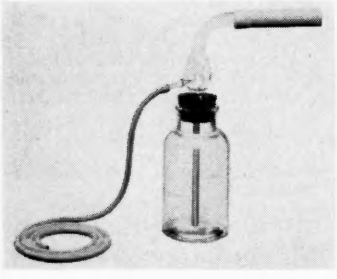
CONTINUOUS-FLOW NEBULIZER COMBINATION



Subscribers to the ANNALS will be interested in the new Continuous Flow Nebulizer Combination No. 840 recently introduced by The DeVilbiss Company, Somerset, Pennsylvania.

This model is specifically designed to meet the increasing demand for prolonged and continuous nebulization. It operates with compressed air or oxygen. The unit consists of a Pyrex glass nebulizer, air tube, fluid tube, vapor extension tube and 500 cc Reagent glass container.

The No. 840 Continuous-Flow Nebulizer Combination will nebulize 500 cc in twenty-four hours with approximately 7 pounds p.s.i., and a flow rate of 6 liters per minute. Nebulization will continue uninterrupted and unattended as long as fluid remains in the container.

The American College of Allergists

By-Laws

BY-LAW AMENDMENTS

At the annual meeting of the Board of Regents held in Chicago in April, 1953, Article VIII of the By-laws, entitled "Amendments" was amended to read as follows:

"At any duly convened regular or special meeting of the Board of Regents these By-laws may be modified, altered or amended by a majority vote of all the members of the Board; these By-laws may also be modified, altered, or amended by a majority vote of all Fellows, present in person or by proxy, at any duly convened annual or special meeting of the College, provided that in each case the proposed amendment or amendments shall have been included in the call of the meeting at which said action is to be taken, and that before the same can be voted upon said proposed amendment or amendments shall have been put in final form by counsel for the College and shall have been published in the official organ of the College."

At the interim meeting of the Board of Directors held at the College headquarters in Minneapolis on December 5, 1953, the Board of Directors by unanimous vote adopted a resolution recommending to the Board of Regents that at its next annual meeting it make and adopt certain changes in and amendments to the By-laws.

Pursuant to the provisions of Article VIII above, as amended, any changes and amendments proposed must first be referred to counsel to be put into final form, after which it is required that the same must be published in the ANNALS OF ALLERGY. Unless these requirements are complied with such proposed changes and amendments cannot be acted upon at either a meeting of the Board of Regents or of the Fellows of the College.

Accordingly, counsel has reviewed these changes and amendments and has approved them as to form. They are hereby published so that they may now appear on the agenda of, and be acted upon at, the next annual meeting of the Board of Regents to be held at Miami Beach on April 4, 1954.

AMENDMENTS PROPOSED

Article V, Section 7 (i) Board of Directors. Second sentence of the first paragraph to be deleted and replaced by the following:

"The Board of Directors shall always be composed of the following officers: the retiring President, who shall be its Chairman, the incumbent President, who shall be its Vice Chairman, the President-Elect, the First Vice President and the Secretary-Treasurer."

Article V, Section 7 (g) entitled "The Nomination of Officers," to be amended to read as follows:

"The Nominating Committee shall be composed of five (5) members: The President, two (2) members of the Board of Regents each of whom has served at least two (2) years on the Board, and two (2) past Presidents, both Regents and past Presidents to be selected by the Board. Not earlier than three (3) months, but not more than six (6) months after its selection the Nominating Committee shall pick one (1) candidate for each elective office and this shall be known as the official ballot. In making its selection it shall take into consideration the qualifications,

fitness, capacity, standing and accomplishments in the field of allergy of those considered for selection, and all information contained in the membership records maintained in the Secretary's office as to any proposed selectees shall be seasonably supplied to the Committee for this purpose. The Nominating Committee shall report its selections to the Secretary-Treasurer's office and as soon as convenient thereafter, but not less than three (3) months before the ensuing election, notice of this official ballot shall be given to all voting Fellows of the College. This notice may be given either by publication thereof in the official organ of the College, ANNALS OF ALLERGY, or by mail. Additional nominations may also be made by petition, signed by ten (10) Fellows and sent to the office of the Secretary-Treasurer, provided said additional nominations are received in the office of the Secretary-Treasurer at least thirty (30) days prior to the next annual meeting. Nominations may also be made from the floor at any annual meeting. The election of officers and Regents shall be by ballot and shall be by a majority of the votes cast at the annual meeting.

Article V, Section 7 (f) The Secretary-Treasurer. The penultimate sentence which reads as follows: "He shall be an ex officio member of all committees and boards" to be deleted therefrom.

Article VI, Section 2, entitled "Finance Committee" to be further amended to conform with a resolution adopted at the interim meeting of the Board of Directors held at the College Headquarters in Minneapolis, Minnesota, December 5, 1953.

PAPERS READ BY TITLE AT ANNUAL MEETING

Unfortunately, there were a number of good papers submitted to the Over-All Chairman of the Program Committee too late for active participation in the program. One or two of these papers may be read, if time permits. Copies of all papers read by title should be presented to the Over-all Chairman of the Program Committee at the time of the meeting. They are then submitted to the Editorial Board for publication in the ANNALS OF ALLERGY, unless otherwise determined by the Editorial Board. In this instance, they will be returned to the author for publication elsewhere.

In Memoriam

ARTHUR J. ABRAMSON

Dr. Arthur J. Abramson, an Associate Fellow of The American College of Allergists since 1946, died suddenly October 27, 1953, in his native city of San Francisco, California, where he was born in 1907. Dr. Abramson was graduated from the University of California in 1933 with an A.B. degree and from the Medical School of that University in 1936. After graduation, he interned at Mount Zion Hospital, 1936-37, and then enrolled as a special graduate student in the Department of Medicine of the University of California and received training in allergy.

Later, Dr. Abramson served as assistant in the medical and endocrinology clinics, Mount Zion Hospital, as well as home-visiting physician of that same hospital. He was a veteran of World War II, having served in England, France, and Belgium. During this period of military service, he served as ward officer in various army hospitals.

Dr. Abramson is survived by his wife, Emily, and a nine-year-old daughter, Lenore. Other survivors include his father, Mr. Harry Abramson, and a sister, Mrs. Melville Gilbert. Officers and members of the College extend sincerest sympathy to the family.

SECTION ON ALLERGY, MEDICAL SOCIETY OF THE COUNTY OF KINGS AND ACADEMY OF MEDICINE OF BROOKLYN

The next regular meeting of the Section will be held at the Society Building on March 18, 1954, at 9:00 P.M. The subject will be "Vascular Allergy" by Leo H. Criep, M.D., Associate Professor of Medicine, Pittsburgh School of Medicine, and Area Consultant, Allergy, U.S.V.A. Hospital. Joseph Harkavy, M.D., Consulting Allergist, Mt. Sinai Hospital, New York, and Assistant Clinical Professor of Medicine, Columbia University, is the discussor.

ONE HUNDREDTH ANNIVERSARY OF DISCOVERER OF ADRENALIN

The late Dr. Jokichi Takamine, who isolated Adrenalin in 1900, was lauded on the one hundredth anniversary of his birth, at Kanazawa, Japan, November 3, 1953, for his scientific discoveries, international trade contacts and great humanitarian interests. Greatest of all Takamine discoveries was his isolation in 1900 of Adrenalin, the first pure crystalline hormone to be made available to the medical profession.

News Items

AIR LINE FARES TO MIAMI

The Eastern Air Lines offer the following information on fares from some of the major cities to Miami and Miami Beach for the benefit of those attending the convention.

Between Miami and—	*Round Trip First Class*	*Round Trip Coach*	*Family Plan Man and Wife First Class**
Atlanta	$ 76.20	$ 50.60	$120.30
Boston	167.00	—	263.60
Chicago	152.40	100.60	240.60
Cleveland	142.50	103.40	225.00
Detroit	149.40	111.80	235.80
New York	145.80	88.00	230.10
St. Louis	139.30	—	219.90

*Monday, Tuesday and Wednesday

The flying time between these points averages about four hours and there are both day and night flights.

Another point of interest is that Eastern has both day and night air coaches to Miami from Chicago and New York. See your local travel agent or write directly to B. R. Griffith, Traffic and Sales Representative, 122 South Michigan Avenue, Chicago 3, Illinois.

PSORIASIS RESEARCH FOUNDATION, INC.

A panel of prominent California physicians have accepted appointment to the medical advisory board of the Psoriasis Research Foundation, it was announced in December by Emil Wachtel, president. They are: Eugene M. Farber, M.D., Director, Division of Dermotology, Stanford University School of Medicine; Maximilan E. Obermayer, M.D., Clinical Professor and Chairman, Department of Dermatology, University of Southern California School of Medicine; Thomas H. Sternberg, M.D., Dermatology Professor, University of California at Los Angeles School of Medicine, and Frances A. Torrey, M.D., Director of Dermatology, University of California Medical School.

It is anticipated the panel will be enlarged as future needs indicate and will include representation of non-specialists.

The Foundation is a non-profit corporation organized to collect funds for research in psoriasis. It will conduct no research itself. Research grants will be made on recommendation of the medical panel.

Membership of the Foundation is composed largely of psoriatics and friends. It is to them that the fund appeal will be made and directed. At present, a general appeal to the public is not contemplated.

Aim of the Foundation is to approach the psoriatic through his or her physician. Doctors are invited to inform psoriasis patients of the existence of the Foundation. A pamphlet is available which will be forwarded to the physician in whatever quantity needed.

Patients are invited to join and support the organization. Membership is $5.00 a year. Donations to launch the research program are welcome in any amount. Headquarters of the Psoriasis Research Foundation is 44 Page Street, San Francisco 2, California.

In addition to Mr. Wachtel, officers are: Edward H. Mossi, executive secretary; Frank E. Blinn, treasurer; Ann Henry, secretary and Rose Atkins, vice president. William J. Scanlon is publicity and public relations director, 515 Hobart Bldg., San Francisco 4, California.

EUROPEAN ALLERGIST REQUESTS CORRESPONDENCE

Dr. Ramon Surinyach, 183 Balmes, Barcelona, Spain, an eminent Spanish and European allergist, has asked that American allergists who have done, or *are doing,* research work in bronchitis in cotton mill workers, communicate with him. Dr. Surinyach speaks and writes English.

POSTGRADUATE COURSE—AMERICAN TRUDEAU SOCIETY

The postgraduate course on Pulmonary Function, sponsored by the American Trudeau Society, in co-operation with the Massachusetts Tuberculosis and Health League, Harvard Medical School, Boston University School of Medicine and Tufts College Medical School, will be held March 22 to 26, 1954, at the Boston City Hospital, Boston, Massachusetts.

SOUTHEASTERN ALLERGY ASSOCIATION

The Southeastern Allergy Association will hold its annual meeting at the Dinkler-Plaza Hotel, Atlanta, Georgia, March 25-27, 1954. Dr. Katharine Baylis MacInnis, 1515 Bull Street, Columbia, South Carolina, is Secretary.

NORTHERN CALIFORNIA SOCIETY OF ALLERGY

The Northern California Society of Allergy has elected the following officers for the year 1954:

President—Lazarre John Courtright, M.D.

Vice President—Minnola Stallings, M.D.

Secretary-Treasurer—Edward Matzger, M.D.

NEWS OF COLLEGE MEMBERS

We are happy to announce that Dr. James A. Mansmann has been awarded the Certificate of Merit for 1952 by the Pennsylvania Allergy Society. This award is given to one of the members who has contributed in some special way to the progress of Allergy in Pennsylvania for the year of the award.

* * *

Dr. I. S. Kahn of San Antonio has been elected an Honorary Member of the Spanish Allergy Society at their recent meeting held in the Canary Islands.

* * *

Dr. Charles William Vivian announces the removal of his offices to 550 West Thomas Road, Patio B-Suite 122, Phoenix, Arizona.

ALLERGIST WANTED

There is an opportunity for a young allergist to locate in a southern city of 100,000 population. Air-conditioned offices are available in a new building for medical specialists. Hospital facilities are ample and extremely modern.

Please direct all inquiries to Assistant Managing Editor, ANNALS OF ALLERGY, 401 LaSalle Medical Building, Minneapolis 2, Minnesota.

BOOK REVIEWS

BLAKISTON'S ILLUSTRATED POCKET MEDICAL DICTIONARY. First Edition. Edited by Normand L. Hoerr, Ph.D., M.D., Henry Wilson Payne, Professor of Anatomy, School of Medicine, Western Reserve University; Arthur Osol, Ph.D., Professor of Chemistry and Director of the Chemistry Department, Philadelphia College of Pharmacy and Science; Samuel W. Chase, Ph.D., Professor of Histology and Embryology, Western Reserve University; Carl C. Francis, M.D., Associate Professor of Anatomy, School of Medicine, Western Reserve University; Marion G. Howell, LL.D., Dean Emeritus and Professor Emeritus of Public Health Nursing, Frances Payne Bolton School of Nursing, Western Reserve University, and Laura E. Moore, Manuscript Editor, The Blakiston Company. 60 illustrations, 16 in color, 8 in full color; washable cover; 1,032 pages. New York: The Blakiston Company, 1952. Price: Plain $3.25, Thumb-indexed $3.75.

This new illustrated medical dictionary (pocket size—7"x4⅝"), with attractive, durable and flexible binding, is most welcome to authors of medical writings as a convenient ready reference which has up-to-date additions to the rapidly growing medical vocabulary. Like no other pocket dictionary, it contains colored illustrations which are grouped together in a 24-page section at the end of the book. There is a key to pronunciation, and definitions are cross-referenced to the various tables which are conveniently grouped in a special section of the appendix. The small difference in price would warrant purchasing the thumb-indexed volume.

GOUT AND GOUTY ARTHRITIS. By John H. Talbott, M.D., Professor of Medicine, University of Buffalo School of Medicine, Buffalo, New York. 92 pages, 32 figures. Price, $4.00. New York: Grune & Stratton, Inc., 1953.

This modern medical monograph represents the author's efforts following approximately ten years of his first treatise on the subject which dealt with laboratory data on uric acid metabolism and clinical impressions of the condition known as gout. During that time, there has been considerable advancement made in the understanding of this metabolic disease, as well as advances in therapy. As an articular disorder, gout has received increasing attention as a biochemical and medical problem.

This monograph attempts to document the significant advances in gout and gouty arthritis with emphasis on the clinical aspects. There are two groups of patients from which the author derived his conclusion, one at the Massachusetts General Hospital and the second series at the Buffalo General Hospital.

All phases of gout and gouty arthritis are discussed, including definitions, heredity, incidence, etiology, intermediary metabolism of uric acid, illustrated by structural formulas, renal exchange of urate, x-ray findings, precipitating agents, complications, associated diseases, diagnosis, prognosis, prevention and treatment. The chapter on treatment is given full consideration. There are excellent photographs of various bones in the body involved. The bibliography is complete for such a small monograph and the index is conveniently arranged.

SCIENCE AND MAN'S BEHAVIOR. The Contribution of Phylobiology. Including the complete text of The Neurosis of Man. Trigant Burrow, M.D., Ph.D. Edited by William E. Galt, Ph.D. 564 pages. New York: Philosophical Library, 1953. Price $6.00.

This book represents an exchange of views with twenty-nine men of science, whose comments and questions are quoted in the present volume. Such noted scholars as A. J. Carlson, C. Judson Herrick, Clyde Kluckhohn, and the late John

Dewey consider fundamental aspects of Dr. Burrow's behavior studies and their far-reaching implications for scientist and layman alike. Dr. Burrow's life has been devoted with unremitting interest in understanding and resolving man's behavioral conflict. Years of study and research led him to the view that man is in urgent need of adopting an objective, inclusive attitude in respect to behavior disorders, individual and social. The development of scientific principles in this field so vital to man's life and effectiveness became the primary aim of his group-analytic studies. In 1948, an unavoidable delay occurred in the printing of his last book, "The Neurosis of Man," and Dr. Burrow took this opportunity to forge lines of communication with outstanding men in various fields of science by introducing certain chapters of his book to them in advance of its publication. In this connection, it should be mentioned that these comments, and Dr. Burrow's response to them, were offered spontaneously and informally and should not be considered as expressing an exhaustive, critical analysis.

OFFICE ENDOCRINOLOGY. Fourth Edition. Robert B. Greenblatt, B.A., M.D., C.M. Professor of Endocrinology, Medical College of Georgia; Chief of Endocrinology, University Hospital; Director of Endocrine Clinic, University Hospital; Consultant to the Surgeon General, U. S. Army. Augusta, Georgia. Foreword by G. Lombard Kelly, President, Medical College of Georgia. 545 pages. 276 illustrations. Springfield: Charles C Thomas, 1953. Price $10.50.

This authoritative fourth edition has been written for practical and clinical application, based on histologic and physiologic studies. It is to serve as a refresher and a guide. Much of the theoretical and experimental data is purposely deleted. Some of the highlights of the fourth edition are: interpretation of tests for pheochromocytoma, diabetes insipidus, Addison's disease; clarification of the adrenogenital syndrome and Cushing's disease; classification of dwarfism and its management; diseases of adaptation; conservative management of endometriosis; abnormal growth and distribution of hair, syndrome of large pale ovaries; indications and contraindications for use of ACTH and cortisone. The subject of dysmenorrhea is carefully studied, classified and treated. The practical knowledge of amenorrhea is stressed; the concept of psychosomatics in hypothalamicopituitary disorders is considered; the simple rules for the practical application of the Friedman test, the management of sterility and the effectiveness of estrogens, are included. Since allergists have an increasing appreciation of the importance of the influence of endocrines on allergic states, they will find this book very practical.

METABOLISM OF STEROID HORMONES. Ralph I. Dorfman, Ph.D., Associate Director of Laboratories, Worcester Foundation for Experimental Biology, Shrewsbury, Mass., and Research Professor of Biochemistry, Boston University, Boston, Mass., and Frank Ungar, Ph.D., Staff Member, Worcester Foundation for Experimental Biology, Shrewsbury, Mass. 170 pages, 53 figures and 48 tables. Reproduced by photo offset and professional mimeographing. Minneapolis, Minn.: Burgess Publishing Company, 1953. Price $4.00.

This volume is intended to serve as a ready reference for the student, as well as the expert in the field of steroid hormone metabolism. A system of acquainting the known facts concerning steroid hormone metabolism is emphasized by presenting the subject from the viewpoints of the source of 100 odd steroids that have been isolated and identified, their biosynthesis, the influence of micro-organisms on steroids, reactions that steroids can undergo without disruption of the nucleus, and the enzyme system of steroid metabolism is suggested, which aids to correlate the known facts and their identification of natural sources. This presentation is aimed to broaden the scope of the investigator so that he may appreciate the possibilities of new and as

yet unidentified steroids. When dealing with isolation of compounds, the authors presented only those works which give definite proof for a steroid structure. Due to the absence of any international agreement for the nomenclature of the steroids, we have adopted the system employed by Fieser and Fieser (1949). A short review of steroid nomenclature is included.

The authors succeeded in keeping this volume concise, with illustrations and tables which summarize the main story. The complete system presented has a feature which may be appealing to some readers. As new steroids are isolated the findings may be noted at the proper place on the proper figure and the references noted on the facing page. This compact volume will no doubt be found useful by nearly every specialist in medicine, including endocrinologists, biochemists, organic chemists, physiologists, pharmacologists, biologists, anatomists, internists, pathologists, obstetricians, gynecologists, oncologists, pediatricians, rheumatologists and veterinarians, a well as students of these professions. The first chapter is devoted to introduction and nomenclature, with eight additional chapters as follows: Steroids isolated from natural sources; Biosynthesis of steroid hormones; Microbiological reactions; Reactions of steroid hormones in mammals; Enzymes influencing steroids; A complete system of neutral steroid metabolism; Relationships between tissue steroid hormones and metabolites in urine and General Comments. There are nine pages of references, as well as a comprehensive index. The format of the book deviates from the average textbook in that its dimensions are larger, with an attractive, durable board cover. This size makes it much easier to use in the laboratory. The publishers are to be congratulated on their unique way of publishing this interesting text.

SALMONELLAE AND SHIGELLAE. Alfred J. Weil, M.D., Department of Bacteriology, The Bronx Hospital, New York, N. Y., and Ivan Saphra, M.D., Department of Bacteriology, The Beth Israel Hospital, New York, N. Y. 252 pages. 29 illustrations. Springfield: Charles C Thomas, 1953. Price $7.75.

This monograph fills a need for easily available, integrated information on technical details of laboratory aspects of Salmonella and Shigella infections in clinical and public health work, and emphasizes current viewpoints and methods. Purposeful laboratory work not only requires the description of methods, which occupies a great part of these pages, but an understanding of the biology of these microorganisms. An attempt is made to supply the basic data concerning the biological position of Salmonellae and Shigellae, as well as the rationale of these procedures. For the successful co-operation of the bacteriologist with the clinician and the epidemiologist, the former needs general information on the clinical and epidemiological aspects of the diseases caused by Salmonellae and Shigellae.

There are fifteen chapters covering Biological and Immunological Properties of Salmonella and Shigella: The Shigellae; The Taxonomy of the Genus Shigella; The Salmonellae; Methods of Isolation; Cultural Methods for the Identification of Shigellae and Salmonellae; The Serological Differentiation of Shigellae; The Serological Differentiation of Salmonellae; The Widal Test, Borderline Organisms and the Question of the Pathogenicity of Other Enterobacteriaceae, Clinical Features and Epidemiology of Salmonelloses and Shigelloses, Natural and Immune Resistance; Vaccination, the Shiga Toxin, Serotherapy; Animal Experimentation; Bacteriophages for Diagnosis and Therapy of Salmonelloses and Shigelloses; Sulfonamides and Antibiotics, and a final chapter on Notes on Cultural Methods, which is detailed and most helpful.

The authors have arranged an excellent index of a difficult subject.

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